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American Journal of Diseases of Children

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THE BLOOD DURING THE FIRST YEAR OF LIFE

II. THE ANEMIA OF PREMATURITY

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AND

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WITH THE TECHNICAL ASSISTANCE OF RAY BENNETT

NEW YORK

That an anemia of variable severity and duration tends to develop in premature infants has long been the general belief among pediatricians. Hess [1] spoke of "an anemia which develops quite regularly and strikingly during the first three months of life." Mackay [2] mentioned the "early and severe anemia" which occurs in all premature infants. Lucas and Washburn [3] stated that premature infants seem particularly prone to the development of a mild degree of anemia during the first six to twelve months of life, and that the erythrocyte count for the average premature infant six months after birth is lower than that of a full term infant at the same age. Parts of this subject have been carefully studied in Germany, and Abt and Nagel [4] recently reported on a series of premature infants in this country.

I. SURVEY OF THE LITERATURE

A. *Blood Elements in Premature Infants.*—1. Erythrocytes and Hemoglobin: The most important studies [5] of premature infants have

From the Department of Diseases of Children, the College of Physicians and Surgeons, Columbia University, the Babies' Hospital and the Sloane Hospital for Women.

1. Hess, J. H.: Premature and Congenitally Diseased Infants, Philadelphia, Lea & Febiger, 1922, p. 68.

2. Mackay, H. M. M.: Anaemia in Infancy: Its Prevalence and Prevention, Arch. Dis. Childhood **3**:117 (June) 1928.

3. Lucas, W. P., and Washburn, A. H.: Diseases of the Blood and Blood Building Organs, Clinical Pedriatics, New York, D. Appleton and Company, 1928, vol. 2, p. 39.

4. Abt, A. F., and Nagel, B. R.: Prophylaxis of the Anemia of Premature Infants, J. A. M. A. **98**:2270 (June 25) 1932.

5. The author, method and hemoglobin equivalent of 100 per cent in grams per hundred cubic centimeters of blood are given in the tabulation.

been made by Kunckel,[6] Lichtenstein [7] and Landé [8] and, more recently, by Herz [9] and Abt and Nagel.[4] Kunckel [6] found that the hemoglobin in premature infants was at high levels in the early weeks of life, that the lowest level was reached between the third month (45.6 per cent) and the fourth month (46.6 per cent), and that the hemoglobin spontaneously reached the level of 53.4 per cent at five months, but he gave no figures after this age. He explained the anemia by the vague hypothesis of "an insufficiency of the hemoglobin metabolism." He did not think that scarcity of iron was the cause of the anemia, since he noted an improvement in one case by "fresh air treatment alone." He obtained an average of 4,085,000 red cells for the first year (exclusive of the first month of life). Lichtenstein [7] found the average hemoglobin of nineteen premature infants to be 40 per cent at the third and fourth months, with an erythrocyte count of 3,616,000 and 2,945,000, respectively. At the sixth month, the average value of the hemoglobin was 40 per cent, and the erythrocyte count was 3,740,000. Lichtenstein [7] believed that the anemia of premature infants is the result of an insuf-

Author	Method	Equivalent of 100 per Cent in Gm. per 100 Cc.
Kunckel [6]	Sahli	17.2
Lichtenstein [7]	Autenrieth-Königsberger and Sahli	17.2
Landé [8]	Sahli	17.2
Herz [9]	Autenrieth-Königsberger	17.0
Abt and Nagel [4]	Newcomer	16.92

ficiency of the hematopoietic apparatus, as well as of the iron reserve. Landé's [8] figures were somewhat higher than those of the two other observers. She found that the percentage of hemoglobin was from 60 to 70 for the period of from six weeks to four and a half months after birth. The erythrocytes were lowest—from 2,900,000 to 3,900,000—at from three to three and a half months. Landé [8] believed that the hypothesis of an insufficient depot of iron in premature infants was supported by her findings that premature infants born at the eighth month of pregnancy in the second quarter of the first year of life showed higher figures for hemoglobin and for erythrocytes than did premature infants born at the seventh month. She felt that this was further proved by the beneficial effect of the administration of iron. In ten premature infants in whom she examined the bone marrow, she

6. Kunckel, D.: Zur Kenntnis der Blutveränderungen bei Frühgeburten und debilen Kindern, Ztschr. f. Kinderh. **13**:101 (July) 1915.

7. Lichtenstein, A.: Hämatologiska studier å för tidigt födda barn under de första levnadsåren med särskild hänsyn till anämiska tillstånd, Svenska läk.-sällsk. handl. **43**:1533 (Dec.) 1917.

8. Landé, Lotte: Beitrag zur Hämatologie, Aetiologie und Therapie der Frühgeburtenanämie, Ztschr. f. Kinderh. **22**:295 (Nov.) 1919.

9. Herz, O.: Haematologische Untersuchungen an Frühgeburten, Monatschr. f. Kinderh. **40**:1, 1928.

found no definite proof that insufficient erythropoiesis is the etiologic factor of anemia of prematurity. Examination of the bone marrow showed a distinct insufficiency of the granulocytic system, which she felt gave a physiologic basis for the premature infant's lack of resistance to infection.

Herz [9] felt that there is a definite difference in the behavior of the blood of full-term infants and of premature infants, and considered a value below 13 Gm. hemoglobin per hundred cubic centimeters an anemic level. Between the ages of 2 and 4 months, sixteen premature infants in his series of one hundred and three infants had a hemoglobin value of from 8 to 12 Gm. Only one full-term infant had a hemoglobin value as low as 12 Gm. Fifteen premature infants of from 4 to 6 months of age had a hemoglobin value of from 8 to 12 Gm. No figures were given for full-term infants for this age group. Herz explained

TABLE 1.—*Results of Study of Blood of Twenty-One Premature Infants by Abt and Nagel*

	Infants of 6 to 7 Months' Gestation		Infants of 8 Months' Gestation	
Age of Infants	Red Blood Cell Count, Millions	Hemoglobin, per Cent	Red Blood Cell Count, Millions	Hemoglobin, per Cent
1 week	6.1	109	6.3	96
2 weeks	5.2	95	6.8	101
4 weeks	5.4	63	5.2	74
6 weeks	3.6	63	4.8	75
8 weeks	3.3	54	4.0	60
10 weeks	3.2	55	4.2	63
12 weeks	3.6	60	3.8	63
4 months	5.0	63	4.7	66
6 months	4.9	68	4.9	79

the anemia of premature infants by an increased destruction and a deficient production of erythrocytes.

Lucas and Washburn [8] stated that the consensus that in premature infants the erythrocytes range from 3,000,000 to 4,000,000 and the hemoglobin from 50 to 60 per cent (the age period was not stated) had been corroborated in his clinic. He thought that the factor of prematurity undoubtedly played some part in interfering with the normal production of red blood corpuscles, and that the general lack of stability of the whole organism which makes premature infants so susceptible to infections and nutritional disturbances must increase the incidence of anemia secondary to such diseases.

Abt and Nagel [4] in a series of twenty-one premature infants found the values to be as given in table 1.

These authors considered that there is an argument against a depleted reserve of iron as an explanation of the physiologic anemia of prematurity, since they stated that prophylactic feeding of iron does not prevent anemia. They felt that the functional incapacity of the hematopoietic system may be analogous to the incomplete and imperfect development of the other systems of the premature infant. Baar and

Stransky [10] stated that the theory of an insufficient depot of iron as the cause of anemia of premature infants is not tenable, and that the anemia is not of alimentary origin but due to a "transitory weakness of the blood-building organs," which also occurs in full-term infants. They believed that there is no pathologic anemia of prematurity, that the same etiologic factors are present in the anemia of premature infants as are present in the anemia of full-term infants, and that the difference is one of degree. Kleinschmidt [11] believed that the anemia of premature infants develops because of defective inheritance; he classed it with that seen in twins, triplets or "feeble infants." Lehndorff [12] stated that the hypothesis of a deficiency in iron is not valid. He felt that the anemia of premature infants is of two types, physiologic and pathologic. The first cannot be prevented by the administration of iron even from birth, and infants recover from it spontaneously even if they are fed milk poor in iron; pathologic anemia does not always improve under medication with iron, but it is cured if infants become strong constitutionally. Meyer [13] divided the anemia of premature infants into two forms: (1) an early form described by Kunckel [6] and Lichtenstein,[7] a true "physiologic" anemia, and (2) a late form, based on Bunge's theory of a depot of iron. Finkelstein [14] also distinguished between a physiologic and a pathologic anemia of prematurity, differentiated chiefly by degree and duration. Baumann [15] studied the association of anemia and rickets in premature infants, and concluded that there was a summation effect of the physiologic anemia of prematurity added to the anemia which he considered was usually found in rachitic infants. He felt that the degree of the anemia was in direct proportion to the degree of rickets present. Van Creveld and Heybroek [16] stated that the high icteric index found for premature infants, which remains high longer than that of the full-term infant, is an evidence of increased and prolonged hemolysis, and that this hemolysis may be one of the causes of the anemia of prematurity. Sanpaolesi [17] made a study of the erythrocytes,

10. Baar, H., and Stransky, E.: Die klinische Hämatologie des Kindesalters, Vienna, Franz Deuticke, 1928, p. 83.

11. Kleinschmidt, H.: Ueber alimentäre Anämie und ihre Stellung unter den Anämien des Kindesalters, Jahrb. f. Kinderh. **83**:97, 1916.

12. Lehndorff, H.: Ueber Anämien im Kindesalter, Monatschr. f. Kinderh. **24**:1, 1922.

13. Meyer, L. F.: Ueber den Einfluss der Ernährung auf das Blut bei Kindern, Deutsche med. Wchnschr. **45**:1345 (Dec. 4) 1919.

14. Finkelstein, H.: Lehrbuch der Säuglingskrankheiten, ed. 3, Berlin, Julius Springer, 1924, p. 752.

15. Baumann, T.: Zur Frage der Anämie bei Rachitis, Monatschr. f. Kinderh. **39**:193, 1928.

16. van Creveld, S., and Heybroek, N. I.: Sur la prophylaxie de l'anémie des prématurés, Rev. franç. de pédiat. **8**:158, 1932.

17. Sanpaolesi, G.: Ueber den Wassergehalt des Blutes beim Frühgeborenen, Jahrb. f. Kinderh. **132**:277 (Aug.) 1931.

hemoglobin and total solids of the blood. In ten infants of eight months' gestation and in two infants of seven months' gestation he found a decrease in the total solids of the blood and an increase in the water content of the blood during the first three months of life. A maximal loss of the total solids of the blood occurred in the third month. With the increase in the water content, the erythrocytes and hemoglobin were found to decrease proportionately, although the weight curve of the blood as a whole did not change. Sanpaolesi concluded that hydremia plays a rôle in the production of the physiologic anemia of premature infants. This is an important observation, which deserves to be studied in a greater number of cases.

2. Platelets: Landé [7] found that the platelets of premature infants ranged from 350,000 to 600,000 per cubic millimeter. Slawik [18] found that nine premature infants at 10 days of age had an average platelet count of 230,000. Keilmann [19] stated that the platelet count of the premature infant is similar to that of the full-term infant; that is, the range is from 48,000 to 168,000. In six premature infants Emmanuele [20] found the maximum to be 680,000 and the minimum 460,000, with a mean of 560,000. In a series of ten premature infants ranging in age from 2 to 63 days, McLean and Caffey [21] found that the average count was 246,000, with a range from 152,000 to 358,000. Beuhamon and Nouchy [22] found that a premature infant of seven months' gestation had a platelet count of 383,000 at birth.

3. Reticulocytes: Luzzato and Ravenna,[23] in studying the reticulocyte count in new-born infants, found the highest count (1.7 per cent) in an infant of seven months' gestation. They stated that the high count found at birth by most observers fell more slowly in premature than in normal infants. Friedlander and Wiedemer [24] asserted that the

18. Slawik, E.: Studien über die physiologischen Verhältnisse des Blutes beim Neugeborenen mit besonderer Berücksichtigung der Blutplättchen, Ztschr. f. Kinderh. **25**:212, 1920.

19. Keilmann, K.: Zur Blutplättchenfrage im Säuglingsalter, Monatschr. f. Kinderh. **23**:383, 1922.

20. Emmanuele, A.: Ricerche sulle piastrine e sulla coagulabilitá del sangue nel neonato, Pediatria **31**:422 (April) 1923.

21. McLean, S., and Caffey, J.: Blood Platelet Counts in Infants and Young Children, Am. J. Dis. Child. **30**:810 (Dec.) 1923.

22. Beuhamon, E., and Nouchy, A.: Les plaquettes sanguines chez le nouveau-né, le nourrisson et le jeune enfant, Compt. rend. Soc. de biol. **107**:171 (May) 1931.

23. Luzzato, A. M., and Ravenna, F.: Ueber die Zahl der vitalfärbbaren roten Blutkörperchen unter normalen Verhältnissen und bei anämischen Zuständen, Folia haemat. **13**:102 (April) 1912.

24. Friedlander, A., and Wiedemer, C.: Basophilic Aggregation in the New-Born, Am. J. Dis. Child. **30**:804 (Dec.) 1925.

blood of premature infants shows a higher percentage of basophilic cells than does the blood of full-term infants, but that the rate of decrease approximated that of normal infants. Frank [25] found from 0.1 to 0.8 per cent reticulocytes during the first weeks of life in premature infants and thereafter a rise to from 3 to 4 per cent. When the erythrocyte count fell to 3,500,000, the reticulocyte count also decreased markedly. A low level lasted only a short time, after which the reticulocytes rose to a level of from 4 to 7 per cent. Later, when the erythrocytes rose, the reticulocytes sank again to a level of from 1.8 to 2.5 per cent. Seyfarth [26] found that four premature infants had from 10 to 30 per cent reticulocytes soon after birth, after which there was a gradual fall. Ockel and Hagen [27] found that fetuses of from four to six months' gestation show high polychromasia. Krafka [28] found high reticulocyte counts, ranging from 26.5 per cent in human fetuses with an estimated age of 3½ months to 6.4 per cent in full-term infants. Since these counts exceed those reported at birth (6.2 per cent), he felt that he had shown that the process of reduction of reticulocytes was initiated long before parturition. He therefore concluded that the changes in the tension of oxygen at birth could not be the primary factor in the reduction of reticulocytes or the controlling factor in erythropoiesis. Salomonsen [29] stressed the fact that the fetus lives in a constant lack of oxygen, a condition similar to that in persons with congenital heart disease and in those who live at a high altitude. At birth the lungs fill with air, and the free supply of oxygen removes the condition on which fetal polycythemia seems to depend. Red corpuscles in excess of those which are needed are removed. Salomonsen concluded that the excess reticulocytes are removed in a similar manner. He found that the reticulocytes are 6 per cent on the day of birth; that they rise to 8 per cent on the fifth day, and that a drop to less than 1 per cent occurs on the ninth day. He reported their disappearance by the seventeenth day. In thirteen premature infants from 1 day to 4 months of age, Moldawsky [30] found that the reticulocytes fell from 4 to 0.7 per cent. In eight older premature infants, aged from 5 to 13 months, he found that the reticulocytes varied from 0.1 to 0.3 per cent. Van Creveld and Heybroek [16] studied

25. Frank, M.: Studien über die Frühgeburtenanämie, Monatschr. f. Kinderh. **37**:468, 1927.

26. Seyfarth, C.: Experimentelle und klinische Untersuchungen über die vitalfärbbaren Erythrozyten, Folia haemat. **34**:7 (April) 1927.

27. Ockel, G., and Hagen, W. W.: Ueber die Polychomasie im roten Blutbild des Neugeborenen, Arch. f. Kinderh. **80**:107 (Jan.) 1927.

28. Krafka, J.: Reticulocytes in the Premature and Stillborn, Folia haemat. **43**:318 (Feb.) 1931.

29. Salomonsen, L.: Physiologic Hematopoiesis and Hemolysis in New-Born Infants, Norsk mag. f. laegevidensk. **91**:1299 (Dec.) 1930.

30. Moldawsky, J. W.: Die praktische Bedeutung der supravitalen Färbung der roten Blutkörperchen, Jahrb. f. Kinderh. **116**:81 (May) 1927.

the reticulocytes in premature infants from the first to the thirtieth week. The percentage at the first week was 2.5, which decreased to the lowest value (0.7 per cent) at the fourth week, with a rise to the highest value (4.5 per cent) at the twelfth week. The number of observations varied from one to six.

4. Coagulation and Bleeding Time: The study of Emmanuele [20] is the only one which deals specifically with premature infants. In six infants he found a maximum coagulation time of one minute and forty-five seconds, a minimum of one minute and a mean of one minute and twenty seconds.

B. *Iron in Its Relation to Anemia.*—The history of the therapeutic use of iron and its relation to anemia are too well known to need more than the briefest survey. Clinical interest in iron followed Bunge's researches in which he propounded the "iron depot theory." This work stimulated investigations into all phases of iron metabolism, only the most important of which are included in the following summary.

1. Iron Storage: In 1899, Hugounenq [31] made an important investigation on the ash of the human fetus at different periods of gestation. He stated that the fixation of iron by the organism is effected during the last three months of pregnancy. During this period the fetus lays down twice as much iron as it has previously deposited, with the result that, according to him, the premature infant is born with a deficient storage of iron. Mackay [32] pointed out, however, that Hugounenq's figures show that the total amount of iron in the ash of the full-term baby is only slightly greater than that of a fetus in from four and one-half to six months. Thus the statement that the store of iron in the premature infant is less in proportion to his weight than that of the full-term infant can be challenged. This small total amount of iron in the fetus has been much commented on in the literature. Mackay [32] contended that the faster the rate of the infant's growth, the lower the hemoglobin level tends to be. She raised the question whether the anemia which so frequently occurs in premature infants is not due to the fact that these infants grow more rapidly in proportion to their weight at birth than do infants of normal weight at birth, thus using up their store of iron more rapidly. Ashby [33] determined the percentage of iron in the livers of one fetus and of six infants of from 2 to 7 months of age, and found that it decreased from 0.058 to 0.013. This

31. Hugounenq, M. L.: Recherches sur la composition minérale de l'organisme, J. de physiol. et de path. gén. **1**:703 (July) 1899.

32. Mackay, H. M. M.: Nutritional Anemia in Infancy, with Special Reference to Iron Deficiency, Medical Research Council, Special Report Series, no. 157, London, His Majesty's Stationery Office, 1931.

33. Ashby, H. T.: The Relation of Iron to Anemia in Infancy and Childhood, Lancet **2**:150, 1912.

percentage of 0.013 was almost the same as that found in the livers of two normal adults, so that he felt that by the time the infant had attained the age of 7 months it had almost exhausted its reserve of iron.

2. Iron Metabolism: Beocker [34] recently showed that the iron content of the liver and the spleen varies in fetuses according to the months of gestation. It is highest at the end of the fifth and at the beginning of the sixth month, lower from the sixth to the eighth month and high again from the eighth to the tenth month. Lichtenstein [35] determined that the iron balance in premature infants is negative, even with an abundant supply of iron. The loss of iron is marked as compared with the reservoir in the body. When a large amount of medicinal iron is given, only a nominal amount is absorbed and retained. It is probable, however, that the iron balance can be made positive by administration of medicinal iron. Lichtenstein [35] gave a ferric chloride solution in milk and found that 50 mg. of iron a day was needed in some cases to make the balance positive. Beck [36] studied the output of iron in two premature infants—from the third and the fourteenth day of life, respectively—for sixty-five consecutive days. Although anemia developed between the second and the third month he demonstrated an increased output of iron which reached a maximum between the thirtieth and fortieth days. He studied the output of iron in three premature infants during administration of iron, and found that most of the iron was eliminated during the period of administration, but that a small part was retained. When the administration of iron was stopped, the retained iron was eliminated. In summing up modern ideas as to the absorption and excretion of iron, Robscheit-Robbins [37] said:

> . . . varying portions of iron are absorbed. The site of absorption is the entire intestinal tract, although the duodenum and a portion of the upper small intestine probably play the major rôle. The absorbed material, either dissolved or in the form of fine colloidal particles, is carried by the blood and to a lesser extent via the lymph passages. This last point might still be considered as open to question. Muller, who questioned Gaule's experiments of thoracic fistula in rabbits, repeated the investigation, employing cats and dogs. Muller's criticism was mainly with the iron solution used, asserting that the mucous membrane of the rabbit is readily injured, and that ferric chloride would easily produce such damage. Muller introduced ferri-oxytartaricum in a weakly alkaline solution by

34. Beocker, P.: Untersuchungen über das vorhandensein darstellbaren Eisens in der Leber und Milz von Föten und Neugeborenen, Centralbl. f. allg. Path. u. path. Anat. **41**:193 (Dec.) 1927.

35. Lichtenstein, A.: Der Eisenumsatz bei Frühgeborenen, Acta pediat. **1**:194 (June) 1921.

36. Beck, O.: Zum Eisenstoffwechsel der Frühgeborenen, Monatschr. f. Kinderh. **51**:418, 1932.

37. Robscheit-Robbins, F. S.: The Regeneration of Hemoglobin and Erythrocytes, Physiol. Rev. **9**:666 (Oct.) 1929.

stomach tube. From two to three hours later, no iron was demonstrable in the lymph. Based on these experiments, Muller concluded that the greatest portion of inorganic iron was transported via the blood stream, and not by way of the lymph. Austin and Pearce suggest that deposition occurs chiefly in the liver, to a lesser extent in the spleen, bone-marrow and perhaps elsewhere. The theory indicated holds good for food iron, organic or inorganic preparations. Elimination is almost entirely by the intestine, especially the colon; very slight amounts are found in the urine and bile. The iron excreted in the urine is usually a very small amount, and is considered to be in firm organic combination according to the belief of Meinertz, although excretion may be considerable if iron is introduced directly into the blood stream. It is generally conceded that the liver is considered to be the main storehouse for iron, both for food iron and for inorganic preparations administered.

Discussing the much debated point as to the relative rôles of the liver and spleen in iron metabolism, Robscheit-Robbins [37] said: "Perhaps the suggestion that both liver and spleen share the function of iron metabolism with the bone marrow may help to smooth matters." Whipple and Robscheit-Robbins [38] said that in anemia one is dealing with the problem of a shortage of iron in the body. Given such a deficit of iron, the body can utilize either organic or inorganic iron.

Mitchell and Schmidt [39] found that different iron preparations vary considerably in their effect, and that the most efficacious are ferric chloride and iron and ammonium citrate. They suggested that the availability of iron be referred to as "soluble versus insoluble," rather than "organic versus inorganic." Williamson and Ets [40] stated that inorganic iron has no therapeutic value in anemia. Mettier and Minot [41] felt that iron is more potent for the formation of blood when absorbed from an acid rather than from an alkaline medium in the intestinal tract. From experiments on dogs, Whipple and Robscheit-Robbins [42] concluded that iron has some effect in the body other than that of mere replacement of iron lost or of worn-out hemoglobin. They held that the effect on the body metabolism is such that more hemoglobin is produced, and they designated this action as a "salt effect."

3. Experimentation with Animals: An enormous amount of work has been done on the production of anemia in animals, and attempts

38. Whipple, G. H., and Robscheit-Robbins, F. S.: Blood Regeneration in Severe Anemia, Am. J. Physiol. **80**:391 (April) 1927.

39. Mitchell, H. S., and Schmidt, L.: The Relation of Iron from Various Sources to Nutritional Anemia, J. Biol. Chem. **70**:471 (Oct.) 1926.

40. Williamson, C. S., and Ets, H. N.: The Value of Iron in Anemia, Arch. Int. Med. **36**:333 (Sept.) 1925.

41. Mettier, S. R., and Minot, G. R.: The Effect of Iron on Blood Formation as Influenced by Changing the Acidity of the Gastroduodenal Contents in Certain Cases of Anemia, Am. J. M. Sc. **181**:25 (Jan.) 1931.

42. Whipple, G. H., and Robscheit-Robbins, F. S.: Blood Regeneration in Severe Anemia, Am. J. Physiol. **92**:362 (March) 1930.

have been made to cure the anemia by diet and by the administration of various metal salts. The most conspicuous of these are the well known experiments of the Wisconsin investigators, Steenbock and his co-workers, on the production of anemia by the method of diet, and those of Whipple and his co-workers on the production of anemia by the bleeding method, followed by attempts to cure the anemia produced. One of the first observations was that of Häusermann [43] in 1897, who deduced from his experiments that animals absorb more iron from a normal diet rich in iron than from artificial feeding of an inorganic iron preparation added to a diet poor in iron. He concluded that there is never any need for medication with iron if the diet is normal.

Iron was given clinically with more or less faith in its efficacy until the experiments of Whipple, Robscheit and Hooper [44] in 1920 showed that pills of ferrous carbonate were inert in dogs made anemic by bleeding which were given diets that did or did not favor regeneration of blood. They stated that they could not assume without proof that inorganic iron is of value in the treatment of secondary anemia. In this same article they made the epoch-making statement that cooked liver is more efficient than muscle in promoting the regeneration of blood. In 1923, McGowan and Crichton [45] found that pigs which were about to farrow and which had been fed a diet without iron for two weeks previously contracted enzootic hepatitis, and that they were immediately cured by being given iron. In 1927, Whipple and Robscheit-Robbins [46] found that an anemia of short duration is not influenced by iron, whereas one of long standing is benefited by iron. In the same year, they also came to the important conclusion that large or small doses of iron salts may cause increased production of hemoglobin, but that by the addition of liver or kidney to iron the sum of the two expected reactions can be obtained. In studying the response of the blood to various iron preparations, Mitchell and Vaughn [47] found that iron and ammonium acetate, albuminized iron, ferric chloride and iron and ammonium citrate were the most efficacious. In 1928, Robscheit-Robbins, Elden, Sperry and Whipple [48] found that the inorganic ash

43. Häusermann, E.: Die Assimilation des Eisens, Ztschr. f. physiol. Chem. **23**:555 (July) 1897.

44. Whipple, G. H.; Robscheit, F. S., and Hooper, C. W.: Blood Regeneration Following Simple Anemia, Am. J. Physiol. **53**:236 (Sept.) 1920.

45. McGowan, J. P., and Crichton, A.: On the Effect of Deficiency of Iron in the Diet of Pigs, Biochem. J. **17**:204, 1923.

46. Whipple, G. H., and Robscheit-Robbins, F. S.: Blood Regeneration in Severe Anemia, Am. J. Physiol. **72**:419 (May) 1925.

47. Mitchell, H. S., and Vaughn, M.: The Relation of Inorganic Iron to Nutritional Anemia, J. Biol. Chem. **75**:123 (Oct.) 1927.

48. Robscheit-Robbins, F. S.; Elden, C. A.; Sperry, W. M., and Whipple, G. H.: Blood Regeneration in Severe Anemia, J. Biol. Chem. **79**:563 (Oct.) 1928.

of beef liver and kidney is half as potent as the fresh preparation. In 1928, Hart, Steenbock, Waddell and Elvehjem [49] made the important statement that copper is highly active in the anemia of rats; they also found that liver and iron together are effective. McHargue, Healy and Hill [50] gave the clinical evidence that after anemic rats had been treated with copper their skin showed a pink ruddiness which was absent in the controls. They concluded that copper has an important function in the formation of hemoglobin and in the metabolism of animals with red blood. Elden, Sperry, Robscheit-Robbins and Whipple [51] found that the iron salt is more effective in the production of hemoglobin than is copper, though copper has a positive effect. They stated that combined copper and iron may have an unusually favorable effect. In 1929, Sperry, Elden, Robscheit-Robbins and Whipple [52] found that there are a number of factors (organic and inorganic) concerned in the effect of liver as studied in simple experimental anemia due to bleeding. They found that a considerable salt effect is demonstrable in watery and alcoholic extracts as well as in residues. They felt that it is impossible to say which salts are wholly responsible, but stated that in the anemia which they studied iron was of more importance than any other inorganic element.

Flinn and Inouye's [53] experiments indicated that copper may play a rôle in stimulating the formation of blood, and that its constant presence in the liver, even in that of the fetus, may not be due only to the fact that this organ is a filter. The oxygen capacity of the blood of guinea-pigs and dogs was increased when copper was fed. Elvehjem and Hart [54] found that in chicks copper acted as a supplement to iron in the synthesis of hemoglobin. Whitehead and Barlow [55] found that in rats fed a strict diet of rice, beef muscle or liver was more effective than iron and copper in curing the anemia. Myers and Beard,[56] giving

49. Hart, E. B.; Steenbock, H.; Waddell, J., and Elvehjem, C. A.: Iron in Nutrition, J. Biol. Chem. **77**:797 (May) 1928.

50. McHargue, J. S.; Healy, D. J., and Hill, E. S.: The Relation of Copper to the Hemoglobin Content of Rat Blood, J. Biol. Chem. **78**:637 (Aug.) 1928.

51. Elden, C. A.; Sperry, W. M.; Robscheit-Robbins, F. S., and Whipple, G. H.: Blood Regeneration in Severe Anemia, J. Biol. Chem. **79**:577 (Oct.) 1928.

52. Sperry, W. M.; Elden, C. A.; Robscheit-Robbins, F. S., and Whipple, G. H.: Blood Regeneration in Severe Anemia, J. Biol. Chem. **81**:251 (Feb.) 1929.

53. Flinn, F. B., and Inouye, J. M.: Some Physiological Aspects of Copper in the Organism, J. Biol. Chem. **84**:101 (Oct.) 1929.

54. Elvehjem, C. A., and Hart, E. B.: The Relation of Iron and Copper to Hemoglobin Synthesis in the Chick, J. Biol. Chem. **84**:131 (Oct.) 1929.

55. Whitehead, R. W., and Barlow, O. W.: Studies on the Anemia of Rice Disease in Rats, Am. J. Physiol. **89**:542 (Aug.) 1929.

56. Myers, V. C., and Beard, H. H.: The Influence of Inorganic Elements on Blood Regeneration in Nutritional Anemia, J. A. M. A. **93**:1210 (Oct.) 1929.

anemic rats 0.5 mg. of iron daily, found that traces of manganese, nickel, copper, germanium and arsenic had a definite supplementary action on the regeneration of hemoglobin. These observations gave experimental verification to older clinical observations that all elements which supplement iron in the regeneration of hemoglobin stand close to it in the list of numbers in the periodic system. In 1930, Drabkin and Waggoner [57] questioned the specificity of copper in the formation of hemoglobin and stated that rats with copper in their ration are no more resistant to anemia due to a milk diet than rats receiving a diet low in copper. Daniels and Forman [58] felt that iron and copper given to infants are without significant influence. Egg yolk was without benefit, and liver increased the hemoglobin content slightly. Wheat embryo extract gave the highest values which they observed in infants. In 1931, Myers and Beard [59] stated that iron is essential for the regeneration of hemoglobin, and that the other metals are probably catalytic. They felt that the specificity of copper as a supplement to iron has little support. Beard, Rafferty and Myers [60] stated that inorganic iron is prophylactic and curative in nutritional anemia. They thought that iron supplemented by copper, nickel, manganese or arsenic is not more effectual than iron alone in preventing anemia. Myers, Beard and Barnes [61] found that certain elements—vanadium, cobalt and germanium—gave polycythemia and hemoglobinemia. They also found that iron alone gave high figures. This observation is interesting in connection with the high figures we found for some of our treated premature infants, as compared with the level in normal full term infants. Beard, Baker and Myers [62] stated that in nutritional anemia of rats the action of iron was analogous to that of liver or liver extract in pernicious anemia. By the administration of 0.25 mg. of iron daily the reticulocytes were raised from 15 per cent to 45 per cent in four days, and there was a slow and gradual increase of erythrocytes and hemoglobin. The chief action of the iron appeared to be the stimu-

57. Drabkin, D. L., and Waggoner, C. S.: Hemoglobin Maintenance and Production Upon Synthetic Diets, Including Modifications in the Ethyl Xanthate and Biazzo Methods for Copper Analysis, J. Biol. Chem. **89**:51 (Nov.) 1930.

58. Daniels, A. L., and Forman, M. B.: Relation of Various Substances Used in the Artificial Feeding Mixtures of Infants to Nutritional Anemia, Proc. Soc. Exper. Biol. & Med. **28**:431 (Dec.) 1931.

59. Myers, V. C., and Beard, H. H.: Studies in the Nutritional Anemia of the Rat, J. Biol. Chem. **94**:89 (Nov.) 1931.

60. Beard, H. H.; Rafferty, C., and Myers, V. C.: Studies in the Nutritional Anemia of the Rat, J. Biol. Chem. **94**:111 (Nov.) 1931.

61. Myers, V. C.; Beard, H. H., and Barnes, B. O.: Studies in the Nutritional Anemia of the Rat, J. Biol. Chem. **94**:117 (Nov.) 1931.

62. Beard, H. H.; Baker, R. W., and Myers, V. C.: Studies in the Nutritional Anemia of the Rat, J. Biol. Chem. **94**:123 (Nov.) 1931.

lation of the hematopoietic organs in the bone marrow to form new reticulocytes. Iron plus copper and other metals gave a more rapid increase in cells and hemoglobin. The action evidently speeded up the maturation of red blood cells. Beard [63] felt that variable rates of recovery under iron therapy are to be expected, because of differences in the initial concentration of hemoglobin, in the utilization of iron and in the daily inorganic supplement, and because of a milk intake below the optimum necessary for recovery. A good correlation exists between increase in hemoglobin and gain in body weight. These two processes take place simultaneously in anemic young rats with iron therapy during the first three weeks. Better growth was obtained when iron was supplemented with other elements than when iron alone was given.

4. Summary of Animal Experimentation: There is some disagreement as to the effect of iron alone on the regeneration of erythrocytes and hemoglobin. Some experimenters believe that it is efficacious; others feel that it is not. There is more agreement on the efficacy of iron and copper in combination, though some observers still doubt the specificity of copper in the regeneration of blood. Practically all investigators are agreed as to the potency of liver in the regeneration of blood, and in the greater value of the fresh preparation as compared with a dried preparation. Many believe that liver and iron in combination are of greater value than either liver or iron alone, in so-called secondary or nutritional anemia.

C. *History of the Prophylaxis and Treatment of the Anemia of Premature Infants.*—Kleinschmidt,[11] in 1916, discussed forty-five cases of alimentary anemia in infants, two thirds of whom were premature. He stated that iron therapy had no effect on the anemia. He cut down the amount of milk given and gave fruit, vegetables and meat, including sieved liver. As far as we know this was the first clinical observation that liver is effectual in anemia. Kleinschmidt [11] recognized no anemia which was due to a deficiency of iron. In 1916, Kunckel [6] cited the case of a premature infant who received no treatment for his anemia other than fresh air. There was an increase in his hemoglobin from 43 per cent to 60 per cent. Kunckel [6] felt that the well known influence of fresh air on metabolism may be the factor which produces this effect in premature infants. Lichtenstein,[7] in 1917, gave ferrous lactate in doses of from 0.5 Gm. to 1.5 Gm. daily, and obtained favorable results. In 1926, Landé [64] gave from 1 to 2.5 Gm. of reduced iron daily to eight premature infants and found a greater increase in hemo-

63. Beard, H. H.: Studies in the Nutritional Anemia of the Rat, J. Biol. Chem. **94**:135 (Nov.) 1931.

64. Landé, Lotte: Zur Eisentherapie der Frühgeburtenanämie, Ztschr. f. Kinderh. **42**:349 (Nov.) 1926.

globin than in erythrocytes from the second to the third month. She found this increase at an age period when her control group showed the greatest degree of anemia. In 1927, Frank,[25] in a discussion of the treatment of premature anemia, said that nothing definite could be determined concerning the effect of iron on hemoglobin, though he thought that an effect on the erythrocytes could be seen. In twins, he found that the one who received iron showed an increase in reticulocytes and a delay in the anemia, as compared with the other twin who received no treatment. In 1928, Herz [65] used liver in the treatment of anemia, in doses of from 10 to 25 Gm. a day. When giving it to an infant aged 8 weeks, who weighed 2,000 Gm., he started with 5 Gm., increasing the dose 1,525 Gm. a day. He found that it was successful in fourteen of fifteen cases, and especially in premature infants. In 1928, Hottinger [66] fed premature infants of from six to eight months' gestation vegetables and fruits, with a reduced milk diet. In addition, he gave a dose of 0.1 to 0.6 Gm. of reduced iron daily, beginning at the second month; he found that it was well borne and considered that it had a specific action. In 1929, Wundt,[67] in an effort to prevent anemia, gave a preparation of dried fish liver, iron and viosterol to six premature infants. She maintained that the preparation was effective, but her figures are not convincing. In the same year Netter [68] also thought this preparation of benefit in anemia of premature infants. Peiper,[69] also in 1929, entertained the belief that it is impossible even with iron, liver and injection of blood to prevent premature infants from becoming anemic. He believed that the anemia of prematurity has a tendency to spontaneous healing. In 1930, Ulmer [70] tried dietary measures and withheld iron from a series of premature infants. He gave vegetables, lemon juice and a vitamin B preparation soon after the first month, and fresh milk between the second and third months. In several cases the hemoglobin was raised by this procedure from 60 to 70 or 75 per cent between the third and fourth months. In

65. Herz, I.: Leberbehandlung der Säuglingsanämien, Monatschr. f. Kinderh. **40**:117, 1928.

66. Hottinger, A.: Ueber die Aufzucht frühgeborener Kinder im Basler Kinderspital und deren Ergebnisse von 1922 bis 1927, Abhandl. a. d. Kinderh. u. Grenzgeb. **20**:1, 1928.

67. Wundt, N.: Die Anämieprophylaxe bei Unreifgeborenen, Deutsche med. Wchnschr. **55**:1512 (Sept. 6) 1929.

68. Netter, H.: Die Anämieprophylaxe bei Unreifgeborenen, Deutsche med. Wchnschr. **55**:1722 (Oct. 11) 1929.

69. Peiper, A.: Erfahrungen bei der Aufzucht von Frühgeburten, Deutsche med. Wchnschr. **55**:310 (Feb. 22) 1929.

70. Ulmer, O.: Die Anämieprophylaxe bei Unreifgeborenen, Arch. f. Kinderh. **89**:272 (Feb.) 1930.

the same year Silberschmidt [71] observed that in premature infants adequately fed during the first year of life reduced iron is not of value. In nine premature infants to whom it was given he found that it increased neither the hemoglobin content of the blood nor the number of erythrocytes. He concluded that the anemia of prematurity is not caused by a deficiency of iron. Josephs,[72] in 1930, stated that liver in combination with iron had been successful in the few cases of premature anemia in which it was tried. He gave iron and ammonium citrate alone to a small number of premature infants from birth, but observed no great benefit. The hemoglobin of the infants fell slightly less rapidly than that of the controls but tended eventually to reach the same low level. In no case was he able to raise the hemoglobin more than temporarily above 70 per cent. He felt that from the first to the fourth month little result from the administration of iron alone is to be expected in premature infants. Copper as an adjunct was not successful, but he felt that it had had an insufficient trial. Stoeltzner [73] recommended the giving of an egg soup to premature infants as a routine measure. As a result, he obtained high values for hemoglobin and erythrocytes, but he gave no figures. In 1931, Schiff and Joffe [74] observed that it is generally agreed that no treatment will prevent or shorten anemia of prematurity, the etiology of which they felt was still obscure. In twelve cases they gave from 10 to 20 drops of a 1 per cent copper sulphate solution over a period of months, and they concluded that the administration of copper has no prophylactic or therapeutic effect, and that anemia of prematurity and alimentary anemia are etiologically distinct. In 1931, Strunz [75] held that liver therapy has only a moderate value in anemia of prematurity which he did not regard as a deficiency disease. He considered that liver is therapeutically less effective than large doses of iron. In the same year, van Creveld and Heybroek [16] found that an extract of liver and a preparation of vitamin D or a combination of reduced iron and vitamin D had a favorable effect in preventing the development and hastening the cure of severe anemia. In 1932, Abt and Nagel [4] concluded that iron, ventriculin or liver fraction alone is of doubtful value in the

71. Silberschmidt, P.: Wirkt Eisen bei der Frühanämie der Frühgeburten, Jahrb. f. Kinderh. **129**:63 (Sept.) 1930.

72. Josephs, H. W.: The Diagnosis and Treatment of the Anemias of Infancy, South. M. J. **23**:1135 (Dec.) 1930.

73. Stoeltzner, W.: Eisuppe als Säuglingsnahrung, Deutsche med. Wchnschr. **56**:4 (Jan.) 1930.

74. Schiff, E., and Joffe, N.: Kupferbehandlung der Frühgeburtenanämie, Klin. Wchnschr. **10**:1946 (Oct.) 1931.

75. Strunz, F.: Zur Leberbehandlung der Säuglingsanämien, Arch. f. Kinderh. **95**:98 (Dec.) 1931.

prophylaxis of anemia of prematurity. They felt that a combination of dried liver extract fraction with iron and ammonium citrate is favorable. Their best results were obtained in a group of premature infants of from six to seven months' gestation, in whom they found the anemia to be more severe than in those of eight months' gestation.

1. Summary of the Prophylaxis and the Treatment of Anemia of Prematurity: Most observers are agreed that anemia in the premature infant cannot be prevented entirely, though there is some diversity of opinion as to the severity of the anemia. The investigators who have reported success with iron in minimizing the extent of the anemia and raising the blood level thereafter have given iron in large doses. Herz [65] is the only authority who has reported success from large doses of liver alone. Several investigators have reported partial success with liver and iron in combination. No success in the prevention of anemia has been reported from the use of copper alone or in combination with iron.

II. SCOPE OF STUDY

To determine the incidence of the anemia of prematurity, the age of onset, the duration and, finally, the cure and possible prevention is the object of this study. The premature infants studied were born in Sloane Hospital. They were followed in the Vanderbilt Clinic; if hospitalization was required, they were admitted to the Babies' Hospital. A few premature infants who were born at home and brought to the Babies' Hospital soon after birth were included. The infants were under our observation throughout the entire study. We have had to contend with the difficulties incident to any study which is made partly in an outpatient clinic, particularly one which draws on such a shifting population as that of New York City. In spite of close following up by the social service department, the mothers sometimes failed to bring their infants regularly to the clinic, or the infant was lost sight of altogether; occasionally the mothers failed to give the medication ordered.

In race and social status the infants of this group were similar to those described in a previous paper. The diet was also similar, except that solid food was usually given at a slightly later age. The method of feeding was as follows: Breast milk was given during the neonatal period in the nursery of the obstetric department. When this was not available, evaporated milk with approximately 5 per cent additional sugar was substituted. The majority of infants when weaned (before the fourth month) were given a dilution of whole milk or evaporated milk, with additional sugar. Viosterol was withheld from a certain number of the infants for a few months, as they were included in a simultaneous study on rickets. Abt and Nagel have assembled the

evidence that viosterol has no effect on the prevention of anemia in full-term infants. Cereal was added from the fourth to the fifth month, vegetable and egg yolk from the fifth to the sixth month, stewed fruit from the sixth to the eighth month and meat in the form of scraped beef from the seventh to the ninth month.

The criteria of prematurity were a length of 45 cm. or less, according to the findings of Schultz [76] and a weight of 2,270 Gm. or under. The obstetric criterion of the estimated months of gestation was not used, as it was felt to be inaccurate. Immature infants were defined as those whose weight at birth was low, above 2,270 Gm., and below 2,720 Gm., and whose length was greater than 45 cm. They did not conform to our criteria of prematurity, and yet it was not possible to treat them as full-term infants. The mothers of all these infants were essentially normal and gave negative reactions to the Wassermann test, or the infants had negative Wassermann or Kahn reactions.

The treated infants received iron in some form, alone or combined with liver, either soon after birth in an effort to prevent anemia or at a later time, after anemia had definitely developed. Untreated infants received no antianemic therapy and were used as controls. The infants studied were divided into the following groups:

1. Premature: (*a*) Untreated (twenty-six)
   (*b*) Treated prophylactically with iron (sixteen)
   (*c*) Treated prophylactically with iron and liver (seven)
   (*d*) Treated after anemia had developed (ten)
2. Immature: (*a*) Untreated (thirty-one)
   (*b*) Treated either prophylactically or therapeutically (nine)

A. *Morbidity.*—We have applied the same criteria of morbidity to these groups of premature and immature infants as have been outlined previously; that is, we have arbitrarily adopted the rule of considering the common infections, such as rhinopharyngitis, otitis or intestinal indigestion as illnesses only when they affected the weight curve on one or more visits subsequent to the visit at which the illness was reported. There may have been a slight loss of weight in the interval at home, but this was more than recovered by the time of the next visit to the clinic. Several of the premature infants gained very slowly, but at no time showed any loss in weight at subsequent visits to the clinic, except that to be specified later. Under such a ruling five, or 4.9 per cent, of ninety-nine infants showed at some time a stationary weight or a failure to gain. Of the six infants who failed to gain steadily, two showed a slight loss in weight from the eleventh to the twelfth month. Two infants failed to gain between the seventh and

76. Schultz, A. H.: Fetal Growth of Man and Other Primates, Quart. Rev. Biol. **1**:465 (Oct.) 1926.

eighth months. One had acute intestinal indigestion, and the other showed only slight rhinopharyngitis. Another infant failed to gain between the eighth and ninth months and had acute intestinal indigestion. Two infants died; one in the hospital, of pneumonia, and one at home from an unknown cause.

Comparing this morbidity rate with that of a group of normal infants described in a previous paper, the incidence of infections in the untreated premature infants is found to be 3.6 times as frequent as that in the normal infants. Comparing the group of untreated immature infants with the group of normal infants, the incidence of infection is four times as great in the former as in the latter. This is in agree-

TABLE 2.—*Incidence of Infections in Five Groups of Premature and Immature Infants*

Type of Infection	Premature, Untreated Patients, 26 Cases		Premature Patients Treated Soon After Birth, 23 Cases		Premature Patients Treated After Onset of Anemia, 10 Cases		Immature Untreated Patients, 31 Cases		Immature Patients Treated Soon After Birth, 9 Cases	
	A*	B*	A	B	A	B	A	B	A	B
Rhinopharyngitis	24	15	36	14	22	7	28	16	6	5
Otitis media	4	2	8	6	5	3	5	4	1	1
Bronchitis	3	3	11	6	..	..	7	6	1	1
Pneumonia	1	1	..	..	..	..	..	..	..	..
Tonsillitis	..	..	2	1	3	3	1	1	1	1
Acute intestinal indigestion	8	8	19	11	10	4	11	6	5	3
Pertussis	1	1	..	..	..	..	1	1	..	..
Measles	..	..	1	1	1	1	..	..	..	..
Diphtheria	..	..	..	..	1	1	..	..	..	..
Parotitis	..	..	..	..	..	..	..	..	1	1
Mastoiditis	..	..	..	..	..	..	..	..	1	1
Poliomyelitis	..	..	1	1	..	..	1	1	..	..
Osteomyelitis	..	..	1	1	..	..	..	..	..	..
Furunculosis	..	..	1	1	..	..	..	..	..	..

* A indicates incidence of infection; B, number of infants affected.

ment with the generally accepted idea that premature and immature infants are more susceptible to infection than normal infants. Comparing the combined groups of untreated premature and immature infants with the combined groups of treated infants, fifty-seven control infants had ninety-five infections, or an average of 1.6 per cent, and thirty-two treated infants had ninety-six infections, or an average of 3 per cent. This is at variance with Mackay's [32] findings in normal infants. She found that those who were treated with iron had 52 per cent fewer infections than those who did not receive iron. The reason for this variance is not apparent. It is a striking fact that in spite of the high incidence of infection there were only two deaths among the ninety-nine infants during the period of observation. On the other hand, in the group of ten older premature infants whose treatment was not started until after they became anemic there occurred forty-three infections, an average of 4.3 each.

III. METHODS

The same methods for the determination of erythrocytes, hemoglobin, platelets, reticulocytes, bleeding time and clotting time were used as described in a previous paper.[77]

The data have been presented in curves similar to those already described, and the statistical formulas used are identical.

IV. RESULTS AND COMMENT

A. *Groups of Untreated Premature and Immature Infants.*—1. Erythrocytes: Chart 1 shows the curve of the erythrocytes in the group of untreated premature infants for the first ten months of life. Our figures were insufficient to include values for the eleventh and twelfth months. It will be seen that the mean value at birth of our group of infants was 5,540,000 (± 80,000)[78] and at the second month 3,910,000 (± 120,000). Although the curve appears to rise, it can be shown that the variations from month to month throughout the remaining months were of no significance statistically, and that the value at the second month was maintained throughout the period of observation. One infant in this group received medication with iron for sixteen days soon after birth, but was included among the untreated infants. Another infant who had a cephalhematoma and was cyanotic, and whose general condition was poor, was given a transfusion on the day after birth.

Chart 2 shows the curve of the erythrocytes in the group of untreated immature infants for the first year. The mean value at birth was 5,810,000 (± 70,000). It fell to 4,040,000 (± 70,000) at the second month, after which the variations throughout the remainder of the first year were insignificant.

In chart 3 the mean erythrocyte curves of the groups of premature and immature infants are superimposed for comparison with the mean erythrocyte curve of normal infants described in a previous paper. It will be seen that the value at birth for normal infants in this series was 5,950,000; that for immature infants, 5,810,000, and that for pre-

77. Merritt, K. K., and Davidson, L. T.: The Blood During the First Year of Life: Normal Values for Erythrocytes, Hemoglobin, Reticulocytes and Platelets and Their Relationship to Neonatal Bleeding and Coagulation Time, Am. J. Dis. Child. **46**:990 (Nov.) 1933.

78. The figure following the ± sign represents the probable error of the mean and not of the standard deviation which is given on the charts. The probable error was calculated from the formula: $\text{P.E.} = 0.6745 \times \frac{\sigma}{\sqrt{N}}$. A difference between the two mean values (M_1 and M_2) has been regarded as statistically significant only when it is at least three times greater than the probable error of the difference, computed according to the following formula:

$$\text{P.E.}\ (M_1 - M_2) = \sqrt{(\text{P. E}_{M_1})^2 + (\text{P. E}_{M_2})^2}$$

mature infants, 5,540,000. The erythrocytes fell more rapidly through the first few months in the premature and immature groups than in the normal. At the second month our values were, for the normal,

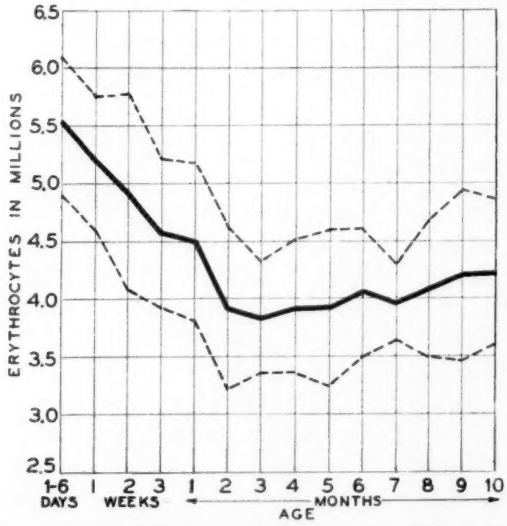

Chart 1.—Erythrocytes of the untreated premature infants through the first year. The charts in this article were made by Mrs. Frances Snipes.

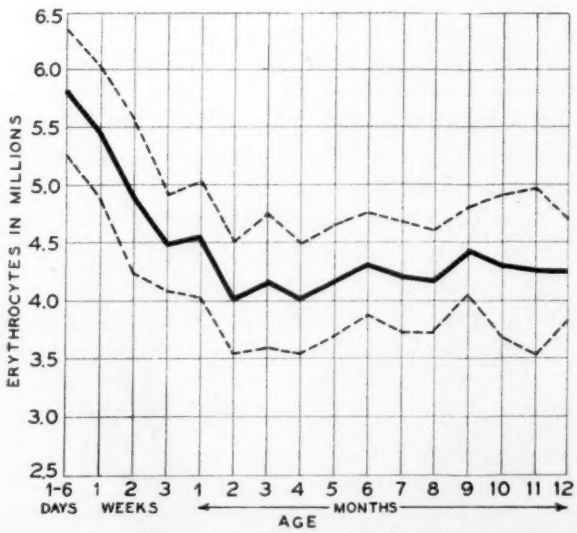

Chart 2.—Erythrocytes of the untreated immature infants through the first year.

4,740,000; for the premature, 3,910,000, and for the immature, 4,040,000. It will be seen that the erythrocytes of the full-term infants remained thereafter at 4,610,000 or above and those of the immature

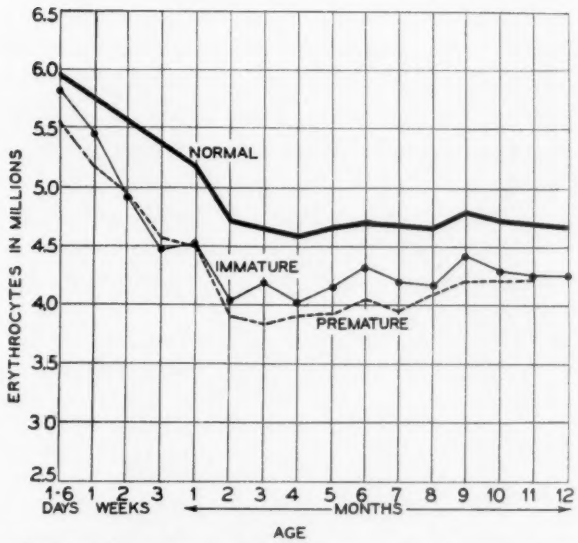

Chart 3.—Comparative mean erythrocyte curves for the normal untreated premature and immature infants through the first year.

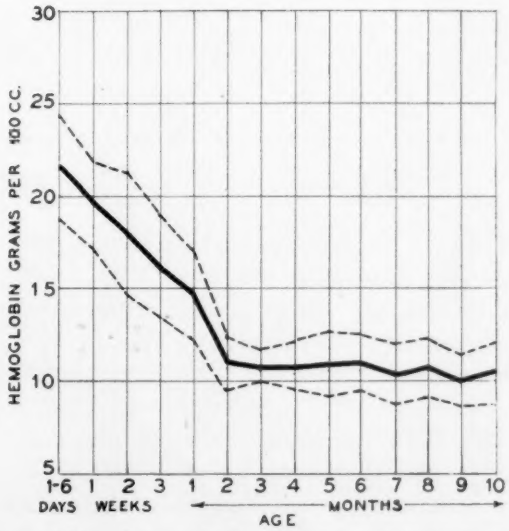

Chart 4.—Hemoglobin of the untreated premature infants through the first ten months.

infants at 4,020,000 or above, whereas those of the premature infants from the second to the seventh month of age remained consistently below 4,000,000, except for a slight rise to 4,050,000 at the sixth month. It has been shown that these slight rises were statistically insignificant.

2. Hemoglobin: Chart 4 shows the curve of hemoglobin of the group of untreated premature infants for the first ten months of life. The mean value at birth was 21.7 (± 0.4) Gm. per hundred cubic centimeters. There followed a rapid fall to the second month with a value of 11 (± 0.2) Gm. per hundred cubic centimeters, after which there was no significant variation throughout the period of observation.

TABLE 3.—*Untreated Premature and Immature Infants*

		Birth	Low Value	Mean‡ (± Probable Error)	Standard Deviation
Erythrocytes, millions	Premature*	5.54 (±0.08)	3.91 (±0.12)	4.00 (±0.03)	0.58
	Immature†	5.81 (±0.07)	4.04 (±0.07)	4.13 (±0.75)	0.56
Hemoglobin, Gm. per 100 cc.	Premature*	21.7 (±0.4)	11.0 (±0.2)	10.8 (±0.85)	1.45
	Immature†	23.0 (±0.4)	11.8 (±0.2)	11.5 (±0.04)	1.50
Reticulocytes, percentage	Premature*	5.2 (±0.34)	0.19 (±0.03)	0.24 (±0.03)	0.20
Platelets, thousands	Premature* Immature†	192 (±5)	304 (±7)	296 (±2)	58.0
Bleeding, minutes	Premature* Immature†	1½ - 2½			
Clotting, minutes	Premature* Immature†	1½ - 4½			

* Figures for premature infants include the first ten months of life.
† Figures for immature infants include the first year of life.
‡ The mean value was derived from an average of the arithmetical means for the various months of the first year, from a point beyond which it was shown that there was no significant variation, according to the formula:

$$M \text{ (group)} = \frac{\Sigma N_a M_a}{\Sigma N_a}$$

The figure for the standard deviation for the first year is computed according to the formula:

$$\text{S. D. (group)} = \frac{\Sigma \text{ (S. D.}_a{}^2 \times N_a)}{\Sigma N_a}$$

Chart 5 shows the curve of hemoglobin of the group of untreated immature infants throughout the first year. The mean figure at birth was 23 (± 0.4) Gm. per hundred cubic centimeters, with a rather rapid fall to the second month with a value of 11.8 (± 0.2) Gm. Thereafter there was no significant difference throughout the rest of the first year.

Chart 6 shows the comparative hemoglobin curves of normal, immature and premature infants. The normal figure at birth was 23.4 Gm.; the immature, 23 Gm., and the premature, 21.65 Gm.

The curves show that the hemoglobin in all three groups followed the erythrocytes in a rather rapid drop to the second month, when the values were as follows: The normal was 13.1 Gm.; the immature, 11.8 Gm., and the premature, 11 Gm. Thereafter, as shown by the

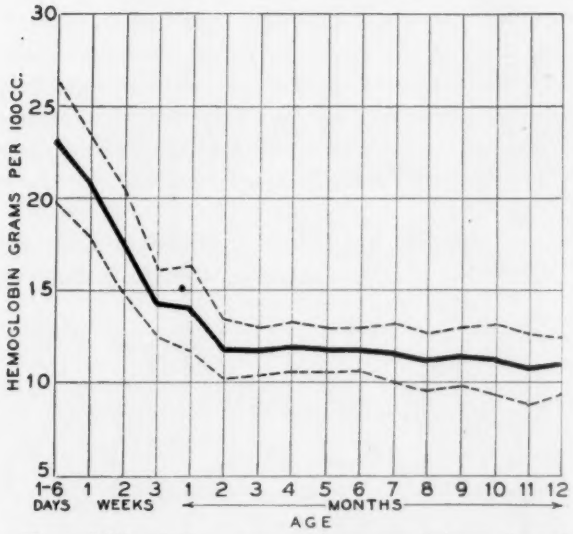

Chart 5.—Hemoglobin of the untreated immature infants throughout the first year.

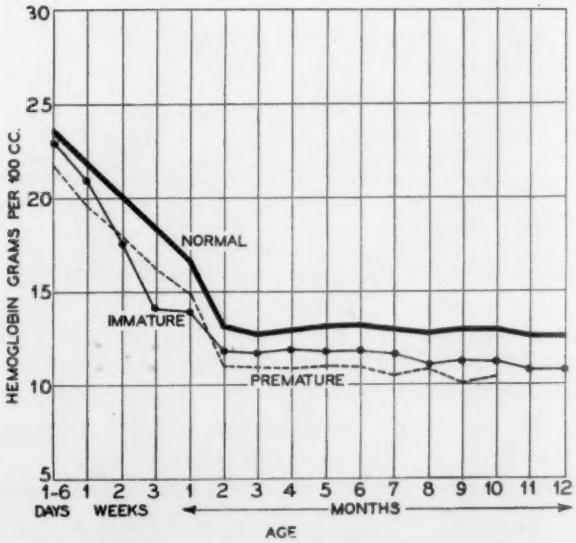

Chart 6.—Comparative mean hemoglobin curves for the normal, untreated premature and immature infants throughout the first year.

curves, the hemoglobin dropped slowly but perceptibly, so that at 1 year the normal figure was 12.4 Gm.; the immature, 10.8 Gm., and the premature, 10.3 Gm. (at 10 months). The chart shows that the hemoglobin curve of the immature infant lies between those of the normal and the premature infant and tends to be nearer that of the premature infant. The curves for both the immature and the premature infants though the first year are definitely lower than that for the normal full term infant.

As previously stated, the theory that the premature infant has a depleted reserve of iron has been questioned by Mackay,[32] and by

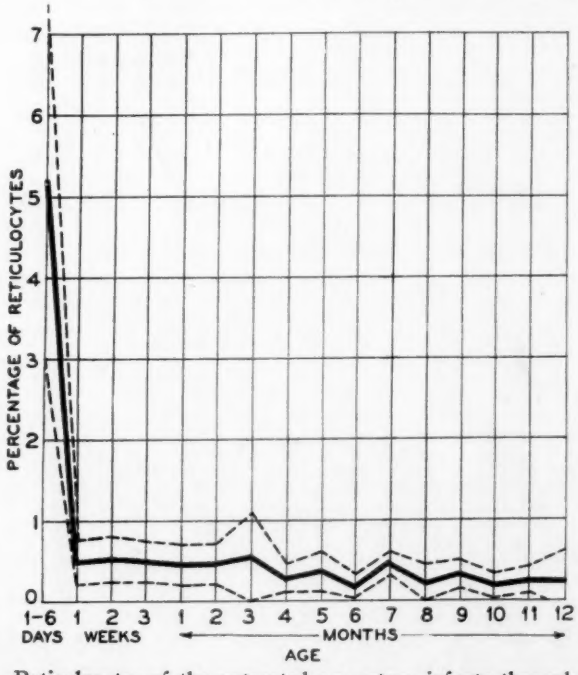

Chart 7.—Reticulocytes of the untreated premature infants throughout the first year.

Hugounenq [31] to judge by her figures for the analysis of ash in fetuses. She pointed out that the amount of iron of the premature infant is very little lower than that of the normal infant, but, as growth is more rapid, the reserve of iron becomes depleted more rapidly. The physiologic drop of the blood seen in the normal infant is exaggerated in the premature infant and occurs probably coincidentally with the depletion of the store of iron. There is probably an added factor in the instability of the hematopoietic system, an instability which it shares with the circulatory and gastro-intestinal systems. This lowered function prevents a sufficiently rapid regeneration of the blood, unless therapy is

resorted to. No more elaborate explanation seems necessary to account for this anemia, which, for the lack of a better term, we shall call physiologic.

3. Reticulocytes: Chart 7 shows the curve of reticulocytes in a group of untreated premature infants throughout the first year. From a percentage of 5.2 (± 0.34) at birth, there was a rapid drop through the first week to 0.48 (± 0.05) and a further gradual fall to 0.19 (± 0.03) at the sixth month. Thereafter the percentage rose sharply to 0.44 (± 0.03) at the seventh month and fell again to 0.22 (± 0.05) at the eighth month. No reason for this sharp variation between the

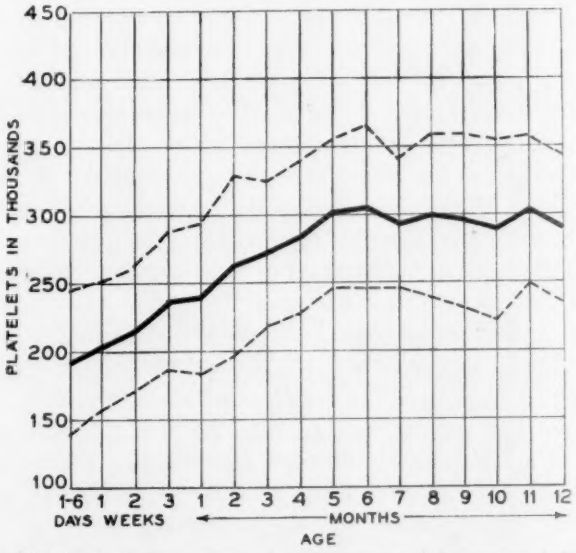

Chart 8.—Platelets of the untreated premature and immature infants through the first year.

sixth and the eighth month can be given. After the eighth month, the minor variations were not of significance. On comparing this curve with that of the reticulocytes of the full-term infants reported on in a previous study it will be seen that the reticulocytes were considerably higher in the premature infants.

4. Platelets: Chart 8 shows the curve of platelets in the combined groups of untreated immature and premature infants. From a figure of 192,000 (± 5,000) at birth, the platelets rose steadily to 304,000 (± 7,000) at the sixth month. Thereafter there was statistically no significant variation in the figures for the rest of the first year, the level lying close to 300,000.

B. *Prophylaxis and Treatment with Iron and with Liver and Iron.*—Iron and iron and raw liver in combination were given to two groups of

premature infants in an attempt to prevent anemia. Iron was given chiefly in the form of iron and ammonium citrate (50 per cent aqueous solution). A few patients received albuminized iron. In charts 10 and 13 we have included two patients who received albuminized iron with those who were given iron and ammonium citrate, as there was no difference observed in the action of the two salts. One infant was changed from one iron preparation to the other during the course of treatment. The dosage of iron and ammonium citrate was 0.3 Gm. per kilogram a day, or 0.05 Gm. of reduced iron per kilogram. Albuminized iron was also used in a dosage of 0.3 Gm. per kilogram a day, which is equivalent to 0.01 Gm. of reduced iron per kilogram.[79] Iron and ammonium citrate was preferred as being easier of administration, though no advantage was noted in the way in which it was tolerated. In most cases the iron was well taken and well tolerated. It practically never caused vomiting. Occasionally diarrhea occurred after the administration of iron, and infrequently a slight amount of blood was present in the stool. This was probably due to an irritation of the intestinal mucous membrane by the iron, as the stools became normal after the medication was terminated. The occasional occurrence of diarrhea after the administration of iron was also noted by Mackay. Iron when given alone was started at from the seventh to the tenth day of life, except in one case in which it was started at the twenty-eighth day. Iron and liver when given in combination was started in the majority of cases at from the seventh to the fourteenth day. The liver was usually started a few days after the iron. Liver was prepared by putting it in its raw state through a meat chopper with the smallest cutting knife. It was then squeezed through gauze and mixed with the formula. The mixture had the consistency of a thin purée. It was well taken as a rule, but diarrhea followed its administration in a few cases. The dose was 5 Gm. per kilogram.

1. Erythrocytes: Chart 9 shows the curve of erythrocytes in sixteen premature infants who received iron prophylaxis soon after birth. The lowest level of the mean curve of erythrocytes was 3,900,000 (± 110,000), which was reached at the second month. It then rose to 5,230,000 (± 100,000) at the sixth month. From the sixth to the

79. The manufacturing chemists who supplied the iron and ammonium citrate and the albuminized iron stated that a similar iron salt previously analyzed contained 0.005 per cent of copper. Therefore 0.3 Gm. of iron and ammonium citrate or albuminized iron would contain 0.000015 Gm. of copper. It is possible that analyses of these particular lots of the iron salts might have had a slightly different percentage of copper. No data are available as to the exact dosage of copper which is effective therapeutically, so we cannot state definitely whether or not 0.000015 Gm. of copper had any effect in our group of cases.

tenth month, there was a fall to 4,710,000 (± 130,000), after which the variations in the curve were not significant.

Chart 10 shows the curve of erythrocytes in seven premature infants who received iron and liver. The lowest level reached by the mean curve of the erythrocytes was 3,850,000 (± 190,000) at the second month. It then rose slightly less sharply than in the group receiving iron alone, to a value of 5,200,000 (± 230,000) at the ninth month. Comparing these two groups, the lowest level of the erythrocytes was approximately the same, and it was reached at the second month. In both groups, the erythrocytes seemed to cross the 5,000,000 line between the fifth and sixth months, but they reached a slightly higher level at the

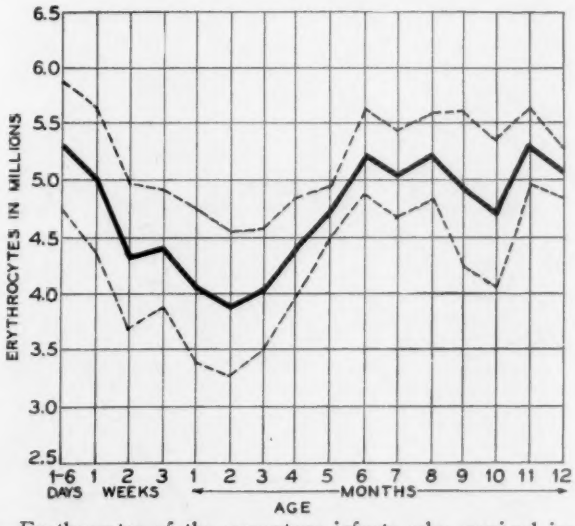

Chart 9.—Erythrocytes of the premature infants who received iron soon after birth.

sixth month in the infants receiving iron alone than they did in those receiving liver and iron.

Chart 11 shows the curve of erythrocytes of premature infants in whom therapy was not started until after they became anemic. At the second month the erythrocytes had fallen to a lower level in this group than in the other two groups, that is, to 3,190,000 (± 50,000), as compared with 3,900,000 (± 110,000) in the group receiving iron and 3,960,000 (± 140,000) in the group receiving liver and iron. While the erythrocytes seemed to continue to fall to the fourth month, this was not of statistical significance. Although the low point in all three groups was reached at the same time (the second month), the high level was reached in the group of anemic infants at a definitely later

time. This would seem to indicate that recovery in infants who receive no treatment before the erythrocytes reach the lowest point is considerably delayed.

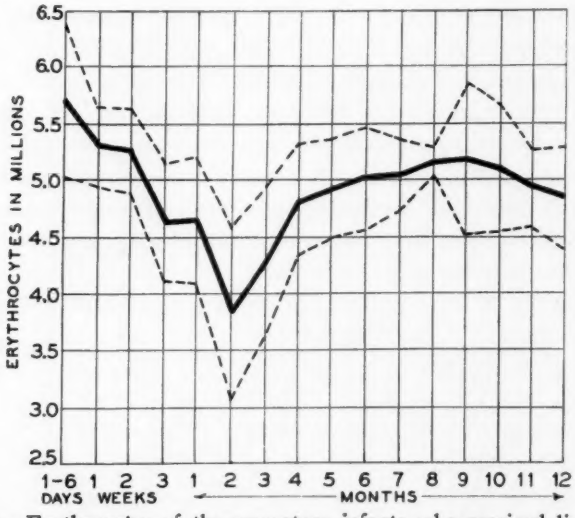

Chart 10.—Erythrocytes of the premature infants who received liver and iron soon after birth.

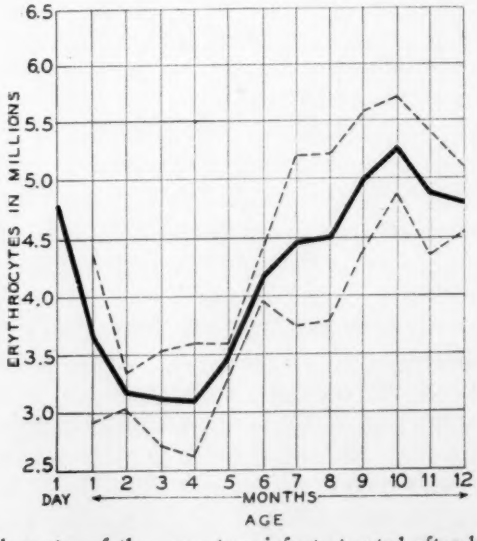

Chart 11.—Erythrocytes of the premature infants treated after becoming anemic.

2. Hemoglobin: Charts 12 and 13 show the mean hemoglobin curves in the two groups of premature infants who received iron and liver and iron, respectively. In both the hemoglobin reached its lowest level at the second month, 11.3 (± 0.3) Gm. per hundred cubic centimeters

in the group receiving iron and 10.9 (± 0.5) Gm. in the group receiving liver and iron. There is no significant difference in these values. The hemoglobin then rose to a slightly higher level—14.7 (±0.3) Gm.—in the infants who received liver and iron than in those who received iron alone—14.1 (± 0.4) Gm., but it did so at a somewhat later time (at the ninth month, as compared with the eighth month in the group receiving iron alone). The advantage of liver and iron in combination, as compared with iron alone, seems negligible in its effect on the hemoglobin.

Chart 14 shows the curve of hemoglobin of the group of infants who were treated after they became anemic. There was a considerably

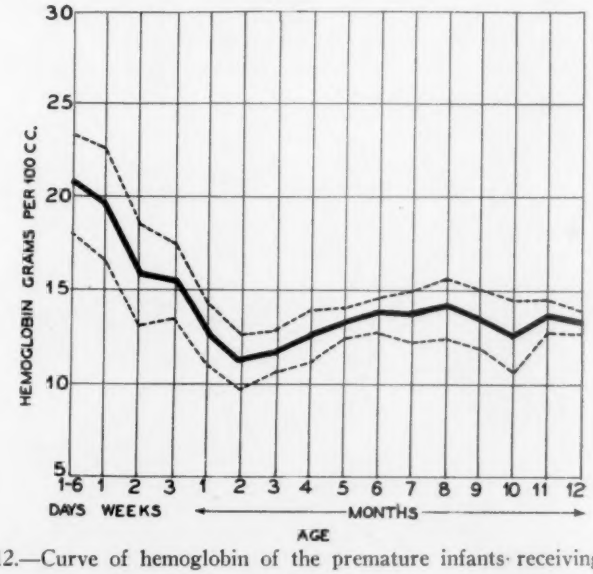

Chart 12.—Curve of hemoglobin of the premature infants receiving iron soon after birth.

greater initial fall (to 9.2 [± 0.2] Gm.) than in either of the groups of patients who received treatment early. The low level in this group was reached at the third month rather than at the second month, as in the other two groups. The rise throughout the remainder of the first year was steady to a value of 13 (± 0.5) Gm. at 1 year. There is no significant difference between this value and that for the group receiving iron—13.3 (± 0.2) Gm.—for the same age period. The infants who received liver and iron prophylactically had a value at 1 year of age—13.7 (± 0.8) Gm.—which was slightly higher than the value for those who received therapy after anemia developed. It is evident, therefore, that though the initial drop in both erythrocytes and hemoglobin could not be prevented altogether, it was less marked in the infants

who received early therapy, and the upward trend began earlier in the treated patients (two months instead of three) and was maintained at a higher level throughout the first year. This remained true in spite of the fact that the therapy was discontinued a few weeks after the high level had been reached. Some writers have reported negative results from therapy, a fact which may be explained by inadequate dosage.

We feel that iron as well as the antirachitic vitamins and orange juice should be given as a routine to all premature infants of from 2 to 3 weeks of age and continued until they have attained 6 months of age, or until the blood reaches a normal level as determined by fre-

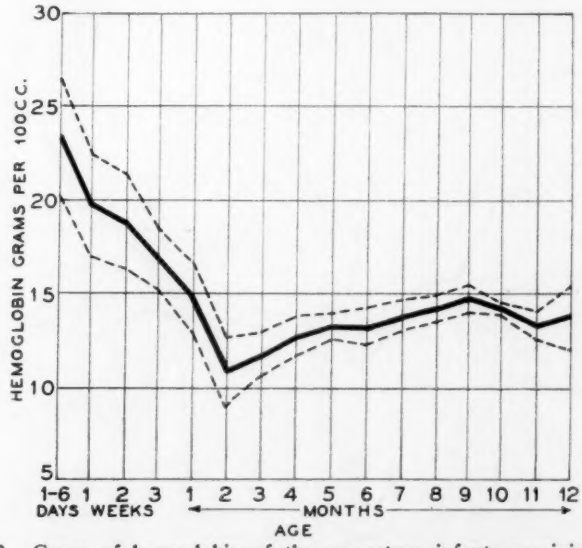

Chart 13.—Curve of hemoglobin of the premature infants receiving liver and iron soon after birth.

quent examinations. In studying individual cases it is noticeable that the low point in the curve comes at varying age periods; also that if the infant has received therapy before the drop comes, the low point is very transitory, and the blood begins to rise immediately. Before this study was undertaken, it was frequently necessary to give transfusions to premature infants, when the erythrocytes had fallen below 3,000,000 and the hemoglobin to 7 or 8 Gm. Prophylactic treatment since the beginning of this work has entirely obviated the necessity of therapeutic transfusion in the premature infant. In comparing the value of iron and liver and iron it seems fair to conclude that liver and iron demonstrate no advantage over iron alone in their effect on either the erythrocytes or the hemoglobin.

3. Reticulocytes: Chart 15 shows the curve of reticulocytes in the group of premature infants treated with iron alone.

Chart 16 shows the reticulocytes in the group treated with liver and iron. There is little difference in the curves for the two groups. Through the first three weeks in the group of patients who received iron alone the reticulocytes decreased less rapidly than in the group receiving liver and iron. It is well known that the response of the reticulocytes to therapy is immediate, and the fact that the infants receiving iron had their medication earlier may account for the difference in the curves during the early weeks. From the first to the fifth month, however, the reticulocytes in the group receiving liver and iron were definitely higher than in those receiving iron alone. It is possible that this was due to

TABLE 4.—*Treated Premature Infants*

	Iron Soon After Birth			
	Birth	Low Value	Mean + (Probable Error)	Standard Deviation
Erythrocytes, millions.....	5.30 (±0.10)	3.90 (±0.11)	4.60 (±0.01)	0.48
Hemoglobin, Gm. per 100 Cc....	20.7 (±0.4)	11.3 (±0.3)	12.75 (±0.1)	1.30
	Iron and Liver Soon After Birth			
	Birth	Low Value	Mean + (Probable Error)	Standard Deviation
Erythrocytes, millions.....	5.70 (±0.19)	3.85 (±0.19)	4.75 (±0.05)	0.52
Hemoglobin, Gm. per 100 Cc....	23.4 (±0.09)	10.9 (±0.5)	13.4 (±0.1)	1.11
	Therapy After Becoming Anemic			
	Birth	Low Value	Mean + (Probable Error)	Standard Deviation
Erythrocytes, millions.....	4.80	3.19 (±0.05)	4.11 (±0.07)	0.75
Hemoglobin, Gm. per 100 Cc....	20.7	9.2 (±0.2)	10.66 (±0.17)	1.77

the effect of liver. From the fifth to the twelfth month there was practically no difference in the two groups of infants.

Herz [65] stated that reticulated cells were relatively increased in the infant's blood, owing to the tendency to revert to the embryonic type; he considered that the increase of reticulated cells observed with liver therapy was not necessarily produced by it, since reticulocytes are often found circulating in the blood after the normal time for their disappearance has passed. Minot, Murphy and Stetson [80] found that a response of the reticulocytes to liver was absent or slight in ordinary cases of "secondary" anemia in adults. Yang and Keefer [81] emphasized

80. Minot, G. R.; Murphy, W. P., and Stetson, R. P.: The Response of the Reticulocytes to Liver Therapy, Particularly in Pernicious Anemia, Am. J. M. Sc. **175**:581 (May) 1928.

81. Yang, C. S., and Keefer, C. S.: The Response of the Reticulocytes in Secondary Anemia Following Various Forms of Treatment, Arch. Int. Med. **45**:456 (March) 1930.

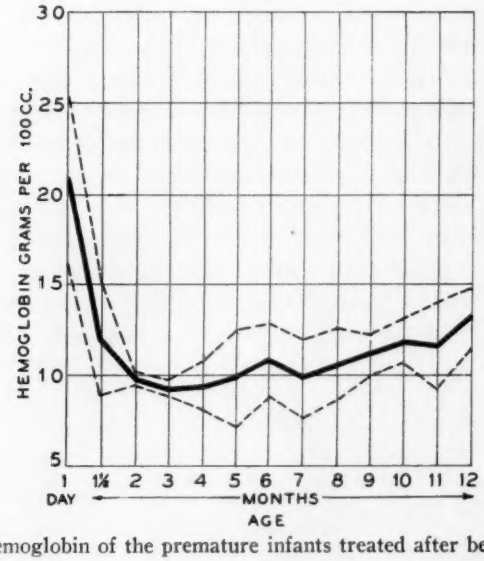

Chart 14.—Hemoglobin of the premature infants treated after becoming anemic.

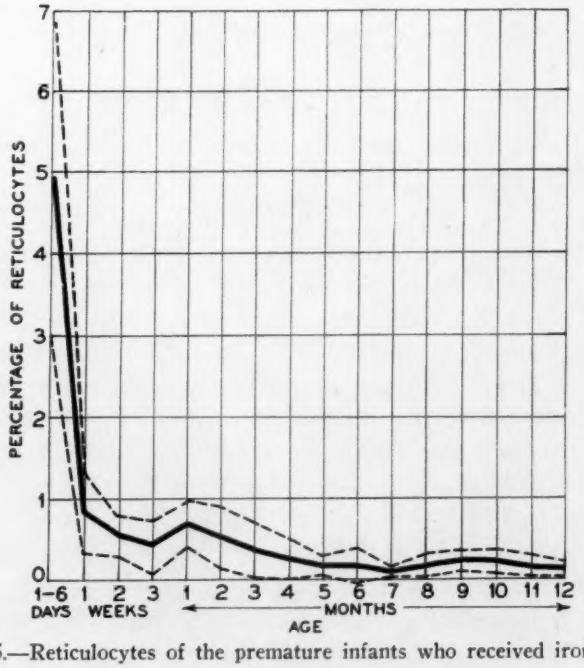

Chart 15.—Reticulocytes of the premature infants who received iron soon after birth.

the fact that the reticulocyte response in adults depended not only on the type of treatment but on the cause and the severity of the anemia. In some cases the reticulocytes were never increased beyond 5 per cent, regardless of the form of therapy or of the severity of the anemia. From their work they felt that liver as a method of treatment was not specific for pernicious anemia, but had a beneficial effect in many forms of secondary anemia. They found that liver and iron in combination was more effective than either iron or liver when given alone. Josephs [72] emphasized that one should be on one's guard against concluding that

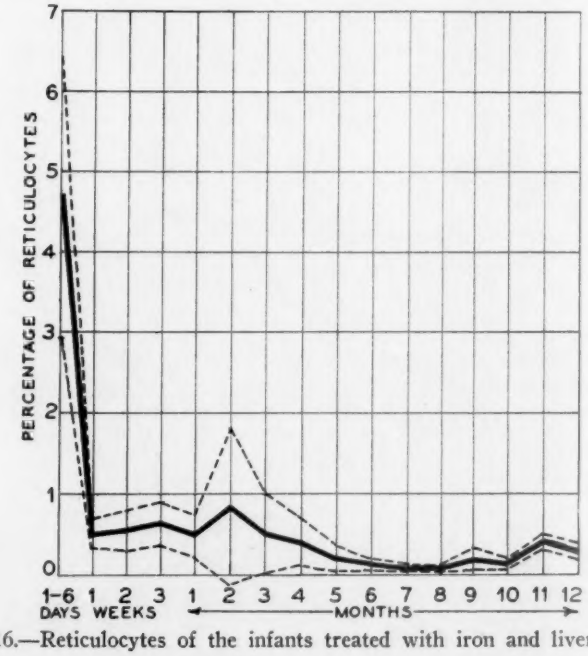

Chart 16.—Reticulocytes of the infants treated with iron and liver soon after birth.

the stimulation of hematopoietic activity did not occur merely because there was no reticulocyte response. Minot and Heath [82] reported a positive response of reticulocytes to the daily oral administration of iron in maximal amounts to patients with anemia due to chronic loss of blood, dietary defects, gastro-intestinal disorders and pregnancy, and to patients with chronic microcytic anemia. They found that the reticulocyte rise was in general inversely proportionate to the level of the red blood cells and hemoglobin directly before treatment, but that the relationships were less exact in the anemias responding to iron than in

82. Minot, G. R., and Heath, C. W.: The Response of the Reticulocytes to Iron, and Some Aspects of Iron Therapy, Tr. A. Am. Physicians **46**:290, 1931.

pernicious anemia responding to liver or to a potent substitute. In this study it was not possible to observe the daily effect of iron or of liver and iron on the reticulocytes, since the majority of the infants were seen in the clinic and since very few were hospitalized. In two cases in which observations were made there occurred an immediate rise in reticulocytes of 6.1 per cent in ten days and 6.3 per cent in five days, respectively. In the first case liver was added to iron previously given, preceding the rise, and in the second case liver and iron were started simultaneously. Another case in which liver and iron were started simultaneously showed an increase in reticulocytes of 4.9 per cent in

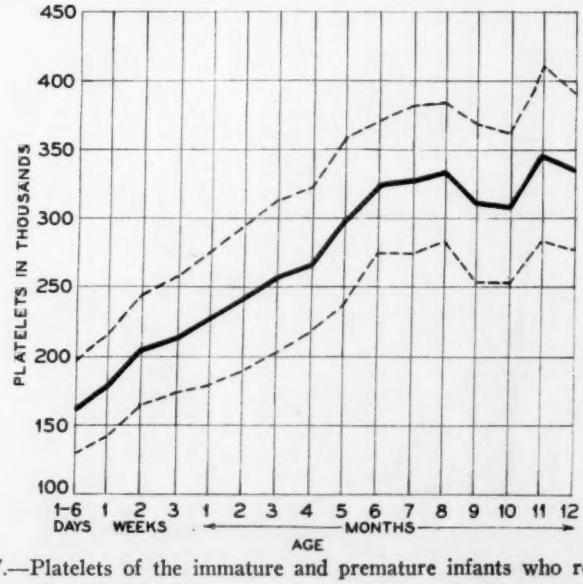

Chart 17.—Platelets of the immature and premature infants who received iron or liver and iron soon after birth.

nine days. From these cases it was not possible to draw conclusions as to whether the response was due to iron or to liver, except in one case in which the reaction closely followed the addition of liver to iron.

4. Platelets: Chart 17 shows the curve of platelets in premature and immature infants who received iron or liver and iron soon after birth. From a figure of 163,000 (± 5,000) at birth the platelets rose steadily to 321,000 (± 7,000) at the sixth month and remained at this level without significant variation throughout the remainder of the first year. Comparison of these figures with those of the untreated patients (chart 8) shows that there was no significant difference in the two groups throughout the first year of life. Therefore no effect on the platelets from treatment with liver and iron can be assumed.

5. Bleeding and Coagulation Time: Chart 18 shows the frequency curves of bleeding and coagulation time at birth of all the premature infants (untreated and treated), and chart 19, that of all the immature infants (untreated and treated). It will be seen that there was little difference between the groups. A majority of the infants had a bleeding time of from one-half to two and one-half minutes and a coagulation time of from one and one-half to four and one-half minutes. Comparing these figures with those for the full-term infants, one notes more variation in the coagulation time of the infants of low weight at birth, while the bleeding time was the same for the two groups.

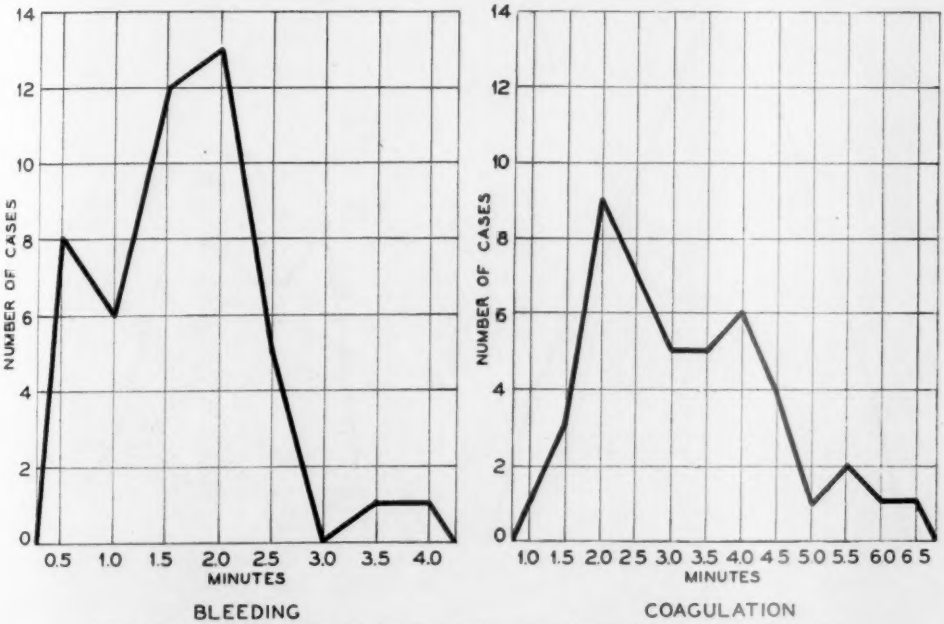

Chart 18.—Curves of the bleeding and the coagulation time in premature infants at birth.

Erythrocyte counts were made and hemoglobin values were determined from month to month for nine immature infants who received therapy at varying times after birth. Eight infants received iron, and one infant received copper and iron. These values are given in detail in table 5.

The erythrocyte counts and hemoglobin values were studied in three sets of premature twins (table 6). One of each pair received prophylactic therapy; the other was used as a control. Twin A of the first pair received iron and ammonium citrate beginning on the tenth day of life. Twin B of the second pair received albuminized iron on the seventh day of life. This was later changed to iron and ammonium citrate. Twin A of the third pair received iron and ammonium citrate on the ninth day of

life. Liver was added on the twentieth day, but it was given irregularly. From the second month on, both erythrocytes and hemoglobin continued to be markedly higher in the treated twin than in the control. In a fourth pair of twins (table 6), both of whom were controls, the erythrocyte and hemoglobin levels were similar and approximated those of the controls.

6. Weight Curves: Chart 20 shows the weight curves of groups of untreated premature and immature infants. It will be seen that their rate of gain throughout the first year was steady and satisfactory. Chart 21 shows the weight curves of treated premature and immature groups.

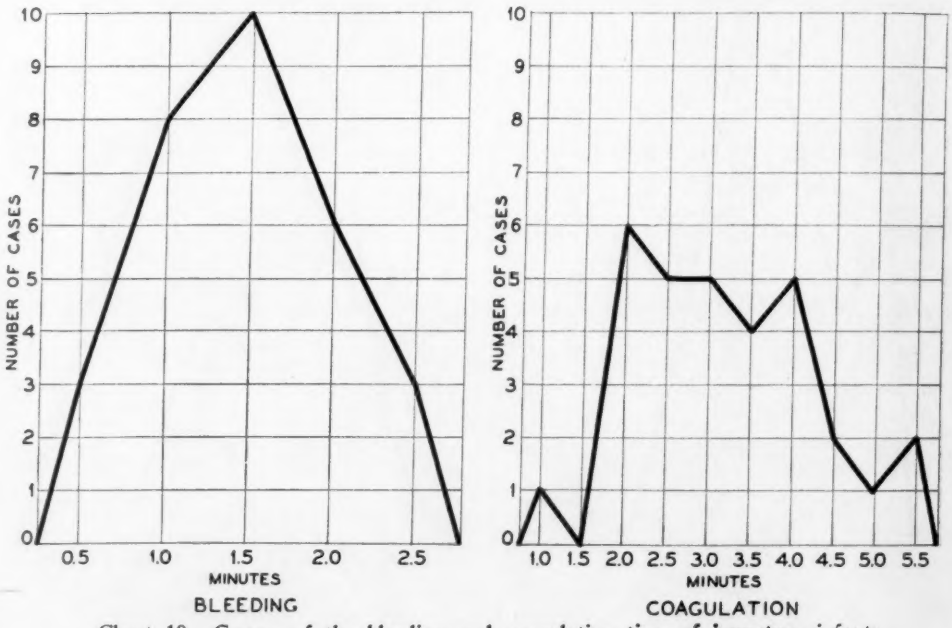

Chart 19.—Curves of the bleeding and coagulation time of immature infants at birth.

These two curves are almost identical. It is therefore to be concluded that antianemic therapy has no influence on weight. This is at variance with Mackay's [32] findings in normal infants. She stated that infants starting to receive treatment with iron at from 3 to 6 months of age were, after three months of treatment, more than 2 pounds (900 Gm.) heavier than the corresponding controls, and that they maintained a superiority of from 2 to 2½ pounds (from 900 to 1,100 Gm.) until the end of observation, at from 9 to 12 months of age.

C. *Other Forms of Therapy.*—Copper sulphate, a 0.5 per cent solution, in Josephs' [72] dosage of 1 cc. per kilogram, was given to three infants. One immature infant with a weight at birth of 2,580 Gm., at 7¾ months of age had an erythrocyte count of 2,970,000 and a hemo-

TABLE 5.—*Treated Immature Infants—Number of Erythrocytes and Percentage of Hemoglobin at the Age Given*

Patient	Beene	Holtzer	Marshall	Hradek	Figueroa	Jusino	Freeman	Hebbons	Grotto
Weight	2,130 Gm.	2,240 Gm.	2,210 Gm.	2,210 Gm.	2,550 Gm.	2,270 Gm.	2,150 Gm.	2,660 Gm.	2,040 Gm.
Treatment	Iron	Iron	Iron	Iron	Iron	Iron	Iron	Iron	Copper and iron
2 days	4,950,000 17.0	.....	5,110,000 20.0	.....	.....	.....	.....	.....	5,320,000 20.0
3 days	.....	4,720,000 20.0	.....	.....	.....	.....	5,250,000 23.0	.....	.....
7 days	4,600,000 17.2	4,650,000 18.0	4,320,000 18.0	5,440,000 17.3	5,700,000 20.0	5,180,000 18.7	5,100,000 21.0	.....	.....
10 days	Iron	Iron							
14 days	3,960,000 13.0	.....	4,400,000 18.0	4,460,000 15.2	.....	5,040,000 16.4	4,780,000 17.3	.....	4,740,000 18.0
21 days	3,530,000 12.0	4,460,000 15.0	3,800,000 13.4	4,300,000 13.0	.....	4,230,000 12.8	4,550,000 18.4	.....	4,060,000 15.4
1 month	2,860,000 9.0	4,500,000 15.0	3,210,000 12.0, iron	3,520,000 11.0	4,300,000 15.0	4,020,000 12.0	2,960 000 10.0	3,700,000 10.0	3,380,000 11.0
2 months	2,770,000 9.2	3,890,000 11.0	3,400,000 10.4	3,090,000 10.0	.....	3,150,000 9.5	2,360,000 8.5	4,410,000 13.0	3,000,000 9.4
2¾ months	.....	.....	.....	Iron					
3 months	3,100,000 10.0	3,670,000 11.0	3,740,000 12.0	3,250,000 10.0	3,680 000 8.7	2,920,000 8.6	3,280,000 9.2	4,400,000 12.5	3,670,000 0.5, copper
4 months	4,300,000 14.0	4,240,000 12.2	3,680,000 12.3	4,250,000 11.5	3,700,000 9.7	3,260,000 8.0	3,000,000 9.0	.....	3,410,000 10.0
5 months	4,750,000 13.5	4,450,000 12.4	4,600,000 14.0	4,170,000 11.0	3,990,000 9.8, iron	3,010,000 6.8	3,000,000 8.0	3,900,000 10.5	3,750,000 12.3, iron
5¾ months	.....	.....	.....	.....	.....	Iron			
6 months	4,810,000 13.4	4,660,000 12.6	.....	4,200,000 12.7	.....	3,380,000 6.7	3,950,000 10.0, iron	4,340,000 12.0	4,680,000 13.6
7 months	5,040,000 13.5	4,720,000 12.5	5,230,000 14.3	4,520,000 14.2	4,450,000 10.5	5,110,000 11.0	4,230,000 11.0	4,410,000 11.5	5,150,000 15.2
8 months	5,210,000 13.0	4,570,000 12.2	.....	4,160,000 12.5	.....	4,900,000 12.0	.....	4,060,000 10.4	5,360,000 15.4
9 months	5,100.000 15.0	.....	5,330,000 14.6	5,020,000 13.8	4,890,000 11.6	.....	.....	3,890,000 10.5	5,210,000 15.6
10 months	5,210,000 15.0	4,820,000 14.0	.....	4,890,000 13.7	5,200,000 14.0	5,090,000 12.5	4,780,000 13.8	3,800,000 10.8, iron	5,260,000 15.5
11 months	5,330,000 14.0	.....	4,880,000 13.0	.....	5,000,000 15.2	.....	.....	.....	5,140,000 14.0
12 months	5,110,000 13.4	4,700,000 12.5	.....	5,050,000 14.0	5,180,000 14.0	.....	5,900,000 16.8	4,230,000 13.0	5,210.000 14.0

TABLE 6.—*Premature Twins, Control and Treated—Number of Erythrocytes and Percentage of Hemoglobin at the Age Given*

	1		2		3		4	
Patient	Control Vetroni B	Treated Vetroni A	Control Leach A	Treated Leach B	Control Solomon B	Treated Solomon A	Control Guttram A	Control Guttram B
Weight	1,960 Gm.	1,930 Gm.	1,900 Gm.	2,020 Gm.	1,960 Gm.	1,730 Gm.	1,670 Gm.	1,440 Gm.
2 days	5,500,000 23.5	4,850,000 19.0	.....	.....	5,680,000 18.5	5,750,000 17.0		
3 days	.....	.....	4,460,000 14.5	5,210,000 17.0				
4 days	.....	.....	.....	.....	.....	.....	5,040,000 21.0	4,810,000 19.5
1 week	4,880,000 20.0	4,350,000 20.0	.....	.....	5,250,000 15.4	5,540,000 16.0	4,500,000 19.2	4,600,000 18.5
2 weeks	4,100,000 17.0	4,000,000 16.0	3,000,000 11.0	3,660,000 10.8	5,460,000 16.5	5,280,000 15.0	4,510,000 21.0	4,550,000 23.0
3 weeks	4,050,000 16.5	4,150,000 16.0	3,210,000 10.7	.....	4,560,000 12.5	5,100,000 14.5	4,260,000 16.0	4,150,000 17.4
1 month	4,100,000 16.0	4,100,000 16.4	3,210,000 10.7	3,850,000 11.0	4,210,000 11.0	5,210,000 14.0	4,150,000 18.5	4,080,000 18.5
2 months	3,230,000 9.7	3,270,000 11.0	3,160,000 10.0	3,350,000 12.0	3,770,000 10.5	4,880,000 12.5	3,860,000 10.0	3,470,000 10.8
3 months	4,300,000 13.0	3,880,000 11.7	3,640,000 10.4	3,810,000 11.2	3,890,000 10.5	4,930,000 13.3	3,700,000 10.6	
4 months	3,400,000 10.0	4,210,000 13.7	3,640,000 10.0	4,120,000 11.8	3,540,000 9.5	5,350,000 14.0		
5 months	3,700,000 11.0	4,720,000 14.5	4,600,000 10.8	4,610,000 13.0	3,530,000 9.0	5,460,000 14.0	3,030,000 9.0	3,270,000 8.8
6 months	3,930,000 11.0	5,140,000 15.0	3,660,000 10.6	4,600,000 12.0	3,550,000 9.2	5,200,000 14.0		
7 months	3,700,000 9.6	5,210,000 14.5						
8 months	3,660,000 9.5	5,120,000 15.0	3,820,000 10.0					
9 months	3,510,000 8.6	5,280,000 14.5	4,120,000 9.5	4,300,000 12.0				
10 months	3,300,000 8.5	4,320,000 13.8	4,440,000 11.2	5,210,000 13.4				
11 months	4,060,000 9.5	5,050,000 13.0	.....	5,050,000 13.5				
12 months	.....	5,240,000 13.6	.....	5,140,000 13.0				

globin content of 7 Gm. Copper treatment was started; in seven weeks the erythrocytes rose to 4,290,000, and the hemoglobin to 9.5 Gm. Another immature infant, weighing 2,055 Gm. at 3 months of age, had an erythrocyte count of 3,670,000 and a hemoglobin content of 9.5 Gm. After the patient had received copper for two months, the erythrocytes were 3,750,000, and the hemoglobin was 12.3 Gm. Iron was added, and in six weeks the erythrocytes rose to 5,400,000, and the hemoglobin to 15.6 Gm. A premature infant of 1,670 Gm. who had an erythrocyte count of 3,470,000 and a hemoglobin content of 11.6 Gm. at 6 weeks of age was given copper for the first time. At 2½ months of age the erythrocytes were 3,130,000 and the hemoglobin 10 Gm. Obviously

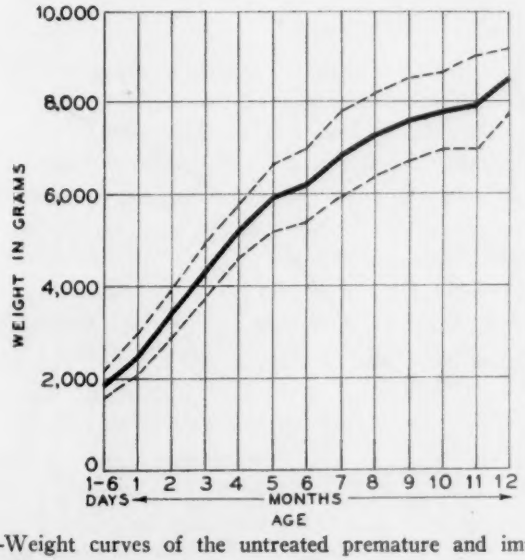

Chart 20.—Weight curves of the untreated premature and immature infants throughout the first year.

no definite conclusions can be drawn from these few cases. Only in the second case was there a decided effect on the hemoglobin, and this seemed to be due to the iron rather than to the copper.

A German proprietary preparation containing dried fish liver, iron and viosterol was given to two premature infants weighing 2,030 and 2,060 Gm. In the first infant treatment was begun at 1 week of age; the erythrocytes were 4,880,000 and the hemoglobin 21 Gm. At 2¾ months of age the erythrocytes were 3,460,000 and the hemoglobin 9.2 Gm. The proprietary was discontinued, and at 3 months administration of iron was started. At 6 months of age the erythrocytes were 4,810,000 and the hemoglobin 12 Gm.; at 7 months, 5,060,000 and 13 Gm., respectively. The second infant was also started on the proprietary at the age of 1 week, at which time there was an erythrocyte count of 5,890,000 and

a hemoglobin content of 25 Gm. Although medication was carried out consistently, there was a fall in both erythrocytes and hemoglobin until the age of 3½ months, when the erythrocytes were 3,960,000 and the hemoglobin was 10.5 Gm. The preparation of dried fish liver, iron and viosterol was stopped at this point, and iron was given. In three weeks the erythrocytes had risen to 5,200,000 and the hemoglobin to 13.8 Gm. The effect of the preparation in the first case was apparently negligible; it is possible that there was some benefit in the second case. From this slight evidence and from other reports in the literature, it seems fair to conclude that the efficacy of the proprietary compound is not comparable to that of iron alone.

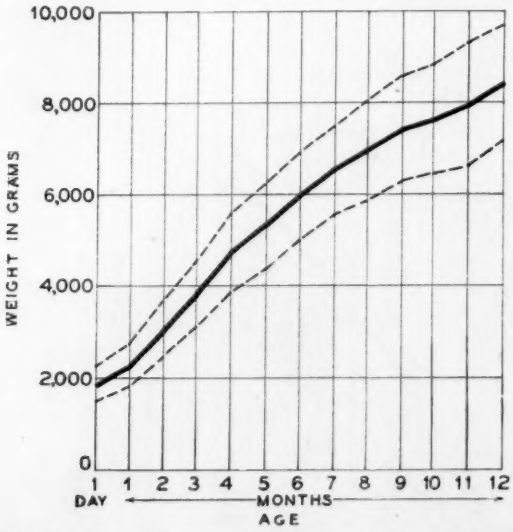

Chart 21.—Weight curves through the first year of premature and immature infants who received iron or liver and iron soon after birth.

When the length of time required to cure anemia in premature infants is to be studied, an accurate estimate of the value of treatment is possible only when the infant is in a hospital where one can be sure that the treatment is given. One premature infant whose weight at birth was 1,280 Gm. had at 10 months of age an erythrocyte count of 2,960,000 and a hemoglobin value of 7.3 Gm. The child was hospitalized, iron and liver were given in large doses, and in less than three weeks the erythrocytes rose to 4,590,000 and the hemoglobin to 12.3 Gm. In nine days the reticulocytes rose from 0.3 to 5.2 per cent. In the clinic it is usually possible to overcome a moderately severe anemia in a premature infant in from eight to ten weeks.

It is interesting to compare the values for erythrocytes and hemoglobin at 1 year of age in the premature infants treated with iron and in the normal infants for whom the statistics were reported in a pre-

vious study. The premature infants showed an average erythrocyte value of 5,050,000 (± 700,000) and an average hemoglobin value of 13.3 (± 0.20 Gm.), whereas those for normal infants were 4,670,000 (± 600,000) erythrocytes and 12.4 (± 0.3) Gm. of hemoglobin. We have commented on the fact that Myers, Beard and Barnes [61] found polycythemia and hemoglobinemia in animals following the administration of iron. Although the figures quoted for premature infants cannot be said to show polycythemic and hemoglobinemic tendencies, it is to be pointed out that at 1 year of age the figures for treated premature infants are appreciably higher than those for normal infants. Whether this higher value is of physiologic advantage can be determined only by further study.

V. SUMMARY

I. A study was made of groups of untreated premature and immature infants as to the behavior of the erythrocytes, hemoglobin, reticulocytes and platelets throughout the first year, and as to neonatal bleeding time and coagulation time. The values at birth and the lowest levels of the erythrocytes, the hemoglobin and the reticulocytes; the value at birth and the highest level of the platelets, and the mean values (table 3, footnote ‡) for all of these elements in the blood after the blood had reached an equilibrium for the period studied are reported. The values for the bleeding and the coagulation time at birth are also reported.

II. A study was made of premature and immature infants who received iron and liver and iron, with respect to their erythrocytes, hemoglobin, reticulocytes and platelets.

1. Premature infants treated with iron or liver and iron after they became anemic showed a greater decline of erythrocytes and hemoglobin and responded more slowly to treatment than did those who received antianemic therapy from birth (table 4).

2. The level of the reticulocytes from month to month in the combined groups of untreated premature and immature infants showed a negligible difference as compared with the level of the combined groups of treated infants.

3. The platelet values for the treated premature and immature infants throughout the first year are reported. No influence of antianemic therapy on the platelets has been found (table 4).

4. This study reiterates the fact that in the majority of premature infants a more or less severe anemia develops. An anemia of milder degree develops in immature infants. This anemia cannot be entirely prevented, but it can be ameliorated by the early administration of iron in large doses. Iron in the form of iron and ammonium citrate (50 per cent aqueous solution) has proved to be a satisfactory preparation in the amelioration and the treatment of the anemia. A dosage of 0.3 Gm. (0.05 Gm. of reduced iron) per kilogram appears to be adequate.

MINERAL GROWTH OF THE HUMAN FETUS

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The mineral growth of the human fetus may be determined from the chemical composition at various stages of fetal development. Data on the chemical composition from which such growth can be shown earlier than the sixth lunar month are, to our knowledge, practically lacking in the literature. This may be due to the difficulty of obtaining sufficient material for the macrochemical methods used by the earlier investigators. In the present study, we were able, using microchemical methods, to study the chemical composition of the human fetus as early as the third lunar month.

In a series of sixteen fetuses, analyses were made for sodium, potassium, calcium, magnesium, phosphorus, chlorine and nitrogen. The analyses of the two youngest fetuses are not complete, since there was not sufficient material for all the microchemical methods. Data which give the per cent of body fat, constant dry weight and per cent of water are also included in this paper. The material for analyses was prepared by bringing the fetus to constant weight in the oven at 98 C. It was then powdered, mixed thoroughly and placed in a desiccator. All analyses were made in duplicate from the dry powdered material.

The material for this study was obtained from the operating room as soon as possible. The length from crown to heel was measured immediately, and the fetus was then weighed. Scammon's [1] formula was used to determine the age in lunar months.

In 1877, Fehling [2] determined the water, ash, fat and protein content of twenty-one fetuses. No analyses, however, were made on the ash to determine the mineral composition. In 1900 [3] and in 1902 [4] Camerer and Söldner made complete analyses of the minerals in six full-term fetuses. In 1900, Brubacher,[5] in Germany, and Hugounenq,[6]

The Bobs Roberts Memorial Hospital and the Department of Pediatrics, the University of Chicago.

1. Scammon, R.: Proc. Soc. Exper. Biol. & Med. **20**:353, 1923.
2. Fehling, H.: Arch. f. Gynäk. **11**:523, 1877.
3. Camerer, W., and Söldner: Ztschr. f. Biol. **39**:173, 1900.
4. Camerer, W., and Söldner: Ztschr. f. Biol. **43**:1, 1902.
5. Brubacher, H.: Ztschr. f. Biol. **27**:517, 1890.
6. Hugounenq, L.: J. de physiol. et de path. gén. **2**:509, 1900.

in France, published data on fetal composition. The latter author presented data from analyses of a series of seven fetuses weighing from 522 to 3,300 Gm. In the same year, Michel [7] also presented data on a 6 month, a 7 month and a full-term fetus. In 1917, Langstein and Edelstein [8] presented data on two fetuses, one 6 and one 7 months of age. In 1929, Hamilton and Moriarty [9] summarized most of these data under two groups, one including the 6 and 7 month fetuses, and the other the full-term.

METHODS

In this study all ashings were done in a muffle furnace at 400 C. From each specimen two samples were taken for ashing. To one sample dilute nitric acid was added and the ash brought to a red heat to oxidize the remaining carbon. The second sample was ashed at 400 C. to prevent loss of potassium, which occurs at higher temperatures. All ashings were dissolved in a 5 per cent solution of nitric acid. Determinations of fat, nitrogen and chlorine were made directly on the dried material. The method described by Holt, Courtney and Fales [10] was used for fat. Nitrogen was determined by the Kjeldahl, and chlorine by the Laudet,[11] method. Sodium was determined by an adaptation of the method of Barber and Kolthoff,[12] and potassium by the method described by Fiske.[13] Magnesium was determined on the calcium filtrate. The supernatant fluid from the precipitation of calcium was evaporated to dryness in a 25 by 250 mm. pyrex test tube. Five-tenths cubic centimeter of ten times normal sulphuric acid was then added, and the excess of oxalic acid was removed by heating. The magnesium was then precipitated as magnesium ammonium phosphate in an alkaline solution of a total volume of 6 cc. The magnesium was calculated indirectly from the phosphorus, which was determined by the method of Fiske and Subbarow [14] on the magnesium salt. Calcium was determined by the method of Fiske and Logan,[15] and phosphorus by the method of Fiske and Subbarow.[14]

RESULTS

In table 1 are presented the values for water, fat and ash according to per cent of body weight for fetuses of various ages. As to body weights for the respective body lengths, Dr. R. E. Scammon, who examined the data, suggested that it should be pointed out that the weights for the determined lengths are somewhat low. However, in

7. Michel, C.: Obstétrique **5**:252, 1900.
8. Langstein, L., and Edelstein, F.: Ztschr. f. Kinderh. **15**:49, 1917.
9. Hamilton, B., and Moriarty, M.: Comparison of Growth in Infancy, Am. J. Dis. Child. **37**:1172 (June) 1929.
10. Holt, L.: Courtney, A., and Fales, H.: Studies in the Chemistry of the Spinal Fluid of Children, Am. J. Dis. Child. **17**:38 (Jan.) 1919.
11. Laudet, M.: J. de pharm. et de chim. **16**:168, 1917.
12. Barber, H., and Kolthoff, I.: J. Am. Chem. Soc. **50**:1625, 1928.
13. Fiske, C.: J. Biol. Chem. **67**:xvi, 1926.
14. Fiske, C., and Subbarow, Y.: J. Biol. Chem. **66**:375, 1925.
15. Fiske, C., and Logan, M.: J. Biol. Chem. **93**:211, 1931.

comparing the series of fetuses in table 1 with his larger series, he found that the weights fall within the zone of the probable errors. There are two reasons for this low weight. In the young fetus the head is very plastic, and elongation of this part of the body may easily account for from 0.5 to 1.0 cm. of error in the measurement of the

TABLE 1.—*Composition of Seventeen Fetuses*

Fetus	Length, Cm.	Age, Lunar Mos.	Weight, Gm.	Dry Weight, Gm.	H_2O, per Cent	Fat, per Cent	Ash, per Cent
18	3.0	2.6	1.7	0.1	95.4		
14	8.0	3.0	18.2	1.1	94.3		
13	9.5	3.2	23.9*	1.4	94.0*		
12	13.5	3.7	59.4*	4.5	92.5*	0.5	1.36
17	17.5	4.3	114.5	12.9	88.7	0.7	1.15
15	23.5	5.1	259.0	32.8	87.3	0.8	1.54
9	25.4	5.4	335.0	41.1	87.7	0.7	2.08
6	27.3	5.7	490.0	60.5	87.6	0.7	2.64
5	30.5	6.2	590.0	85.7	85.5	1.2	2.68
8	31.5	6.4	570.0	82.7	85.5	1.3	2.37
11	36.1	7.2	1,010.0	146.3	85.5	2.2	2.17
1	38.5	7.6	960.0	162.1	83.1	2.2	2.71
10	38.6	7.7	1,205.0	211.4	82.5	3.5	2.40
2	41.3	8.2	1,555.0	316.9	79.6	4.8	2.43
4	41.7	8.2	1,545.0	275.4	82.2	3.4	2.57
3	42.5	8.4	1,615.0	306.6	81.0	3.9	2.47
7	51.8	10.0	2,915.0	714.0	75.5	6.7	3.15

* Corrected for water loss.

TABLE 2.—*The Mineral Composition of the Human Fetus Expressed in Millimols* *

Fetus	Age, Lunar Mos.	Sodium	Potassium	Calcium	Magnesium	Phosphorus	Chlorine	Nitrogen
18	2.6	....	....	....	....	....	....	0.7
14	3.0	0.9	0.2	0.4	....	0.5	....	.....
13	3.2	0.8	0.2	1.0	....	0.9	0.5	11.3
12	3.7	4.5	1.7	2.8	0.3	3.3	3.4	33.2
17	4.3	11.6	4.9	9.1	0.7	7.9	8.7	96.7
15	5.1	26.9	11.2	31.5	2.0	28.7	19.7	247.0
9	5.4	31.3	13.1	39.3	2.6	35.4	24.8	306.0
6	5.7	50.5	18.0	81.6	4.2	66.0	33.9	437.0
5	6.2	55.9	23.4	96.9	4.3	78.4	41.2	626.0
8	6.4	53.5	22.4	80.2	4.6	70.5	40.9	606.0
11	7.2	83.7	39.0	125.1	5.7	111.1	62.9	1,042.0
1	7.6	98.4	35.8	169.1	8.2	130.5	64.0	1,169.0
10	7.7	104.8	56.3	169.9	10.0	147.8	81.3	1,321.0
2	8.2	127.2	66.7	233.4	14.4	203.4	99.7	1,898.0
4	8.2	136.0	67.0	225.6	15.0	200.7	99.3	1,811.0
3	8.4	143.3	71.7	240.0	12.9	211.6	102.1	2,003.0
7	10.0	240.4	125.4	608.4	32.2	482.8	149.2	4,102.0

* A millimol is taken as the number of milligrams equivalent to the atomic weight.

length. If the fetus is not obtained for analysis at once the rapid loss of water which takes place immediately after delivery may also change the relationship of height and the weight.

Table 2 shows the absolute mineral composition of the human fetus expressed in millimols. A millimol in all instances is taken as the number of milligrams equivalent to the atomic weight.

Table 3 shows the nitrogen and mineral composition of the human fetus in millimols per unit of body weight. This table indicates the increase of these substances in the fetus from the third to the tenth lunar month. It is apparent that there is little change in the mineral composition per unit of body weight between the fifth and the eighth lunar months. Later there appears to be a definite increase in the calcium and phosphorus contents. There is, however, a gradual increase in nitrogen up to and including the end of gestation.

TABLE 3.—*The Mineral Composition of the Human Fetus in Millimols per Kilogram of Body Weight*

Fetus	Age, Lunar Mos.	Sodium	Potassium	Calcium	Magnesium	Phosphorus	Chlorine	Nitrogen
18	2.6	....	....	....	....	....	....	405
14	3.0	50.0	8.7	24.1	....	30.4	....	...
13	3.2	34.5	8.2	43.5	....	39.6	21.1	617
12	3.7	76.4	27.8	47.7	4.6	54.4	56.4	559
17	4.3	101.1	42.7	79.3	6.2	69.3	77.0	844
15	5.1	103.7	43.1	121.8	7.5	110.9	76.1	954
9	5.4	94.4	35.5	117.6	7.7	105.2	73.9	907
6	5.7	103.3	36.8	166.6	8.5	134.0	69.1	893
5	6.2	95.3	39.6	164.3	7.3	132.3	69.9	1,064
8	6.4	94.4	30.4	140.8	8.1	123.1	71.9	1,064
11	7.2	83.0	38.5	123.6	5.6	109.5	62.0	1,031
1	7.6	102.5	37.2	176.1	8.6	135.9	61.6	1,221
10	7.7	87.6	46.8	141.1	8.3	122.1	67.4	1,097
2	8.2	82.0	43.0	150.0	9.2	130.2	64.0	1,221
4	8.2	88.5	43.4	146.1	9.7	129.3	64.3	1,171
3	8.4	89.2	44.5	148.6	8.0	130.4	63.2	1,243
7	10.0	76.2	43.2	206.7	11.1	164.9	51.5	1,407

TABLE 4.—*The Mineral Composition of the Human Fetus in Millimols per Kilogram of Dry, Fat-Free Substance*

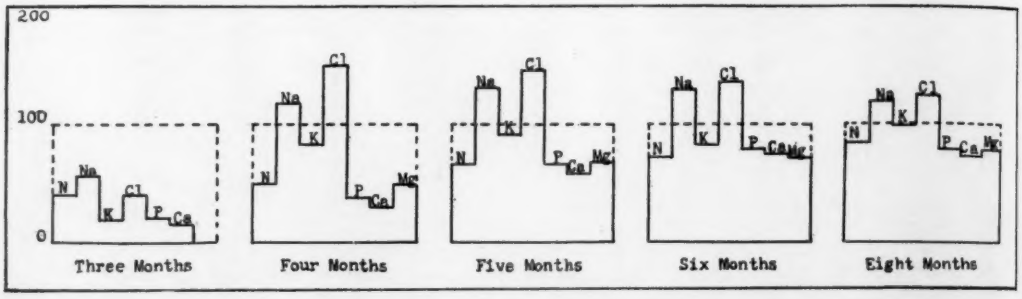
Fetus	Age, Lunar Mos.	Sodium	Potassium	Calcium	Magnesium	Phosphorus	Chlorine	Nitrogen
14	3.0	910	158	439	....	549	...	.....
13	3.2	630	150	798	....	726	387	8,692
12	3.7	1,071	393	676	65.0	772	798	7,905
17	4.3	950	402	746	57.3	648	713	7,928
15	5.1	879	366	1,029	65.3	938	644	8,072
9	5.4	809	339	1,016	67.1	915	641	7,907
6	5.7	886	316	1,432	73.6	1,158	595	7,672
5	6.2	710	297	1,231	54.6	996	523	7,957
8	6.4	710	297	1,065	61.0	936	543	8,050
11	7.2	673	313	1,005	45.8	893	506	8,374
1	7.6	700	255	1,203	58.3	929	456	8,322
10	7.7	620	333	1,005	59.2	875	481	7,824
2	8.2	524	275	962	59.3	838	411	7,819
4	8.2	612	302	1,016	67.5	904	447	8,153
3	8.4	588	294	984	52.8	868	419	8,211
7	10.0	463	241	1,171	62.0	929	287	7,894

Table 4 presents the same data, but values are based on a unit of dry, fat-free substance. As growth takes place, variation is seen in only the sodium and the chlorine, which appear to decrease. This change may be explained most probably by the marked loss in body water.

Table 5 is included to show how well our data in many instances compare with the values collected by Hamilton and Moriarty.[9]

TABLE 5.—*Group Comparison of Mineral Composition in Millimols per Kilogram of Body Weight*

	Sodium	Potassium	Calcium	Magnesium	Phosphorus	Chlorine	Nitrogen
7 premature infants, aged 6 to 7 months, literature [9]	96±3.7	42±1.1	161±6.7	9±0.41	125±4.9	67±4.7	1,179±25
4 premature infants, present data	94±4.4	36±1.8	149±8.8	7±0.56	125±4.9	68±1.9	1,013±35
9 full-term infants, literature [9]	75±3.6	42±1.6	204±14	8±1.0	153±6.8	50±1.6	1,436±40
1 full-term infant, present data	76.2	43.2	208.7	11.1	164.9	51.5	1,407



Fetal composition per kilogram of body weight at 3, 4, 5, 6 and 8 months, compared with the composition of the full-term infant, taken as 100 per cent.

The chart illustrates in a graphic manner the changes in growth as determined from the body composition. It becomes apparent that calcium, phosphorus and magnesium, minerals found in the skeleton of the human fetus, show a gradual increase, while sodium and potassium, found in the intracellular fluid and plasma, show marked fluctuations.

SUMMARY

1. The mineral and the nitrogen content of sixteen fetuses were determined by microchemical methods.

2. In the human fetus the most marked changes in growth in respect to minerals appear to occur in the fourth lunar month.

Dr. F. L. Adair of the Chicago Lying-In Hospital provided material for this study.

FOUR YEARS' EXPERIENCE WITH EXAMINATION OF MATERIAL OBTAINED BY GASTRIC LAVAGE

I. DEMONSTRATION OF TUBERCLE BACILLI AND ITS SIGNIFICANCE IN PROGNOSIS, THERAPY AND ESTIMATION OF DANGER OF INFECTION

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In 1928, in the Children's Hospital, Fugelbakken, we commenced to look for tubercle bacilli in the material obtained by gastric lavage from children with positive tuberculin reactions. Similar examinations have since been carried out in several other hospitals in Copenhagen and in the country. The chief physicians in the departments and hospitals have given us their material for collective investigation.

Addition of the figures for all the hospitals showed 756 children, of whom 235 were discharging bacilli. Many of these were repeaters, however, who had been under treatment in several departments. The actual figures are therefore considerably smaller: In all, 622 children were examined, 199 of whom showed the presence of tubercle bacilli in the material obtained by gastric lavage. All these children gave a positive tuberculin reaction.

The method employed for these examinations was described originally by Meunier;[1] it was adopted by Armand-Delille and Vibert[2] and later by Poulsen, Jensen and Husted,[3] who supplemented it with cultivation on substrates and inoculation of guinea-pigs.

In this study all the bacteriologic examinations, with a few exceptions, were carried out in the tuberculosis department of the State Serum Institute. This gave a uniformity of examination which increases considerably the value of the results.

Aided by a grant from the P. Carl Petersen Foundation.

From the Children's Hospital, Fuglebakken, and the State Serum Institute.

1. Meunier: Presse méd. **2**:81, 1898.

2. Armand-Delille and Vibert: Presse méd. **36**:402, 1927. Armand-Delille: Pulmonary Tuberculosis in Infants, Am. J. Dis. Child. **34**:547 (Oct.) 1927.

3. Poulsen, V.; Jensen, K. A., and Husted, E.: Demonstration of Tubercle Bacilli in Small Children with Pulmonary Tuberculosis, Am. J. Dis. Child. **37**:900 (May) 1929. Poulsen, V.: Ugesk. f. læger **91**:541, 1929; Acta tuberc. Scandinav. **4**:359, 1929; Jahrb. f. Kinderh. **125**:206, 1929.

In order to reduce the expenses connected with these examinations and at the same time to improve the chance of finding bacilli, the lavage was done two days in succession in many cases, the two portions of liquid obtained being put together for examination.

Table 1 gives the results of examination for tubercle bacilli in the entire group according to age. On gastric lavage, the bacilli were found in 199 children, the great majority of whom were within the first three or four years of life. After this age there was a marked fall in the number of positive results.

Sixty-two children were examined during the first year of life, the youngest being from 1 to 2 months old, and bacilli were demonstrated in 54 of these. In the second year of life bacilli were demonstrated in about one half of the patients examined; in the third year, in about one third; in the fourth year, in about one fifth.

TABLE 1.—*Results of Examination for Tubercle Bacilli in Gastric Lavage According to Age*

Age, Years	Tubercle Bacilli Positive	Tubercle Bacilli Negative	Total
0-1	54	8	62
1	50	58	108
2	38	81	119
3	18	76	94
4	7	49	56
5	11	33	44
6	5	26	31
7	8	37	45
8	3	27	30
9	3	18	21
10	2	10	12
Total	199	423	622

Unquestionably, the reason why so many infants under 1 year of age discharge bacilli is to be found in the pathogenesis of tuberculosis in infancy and its tendency toward progression in the first year of life. The children are infected by way of the respiratory passages. Food as a source of infection is disregarded, as tuberculosis from this origin does not play any particular rôle in the frequency of infantile tuberculosis in Denmark; in Copenhagen it is only in exceptional cases that the children are given raw milk. Tuberculous bronchitis or bronchopneumonia develops, and from this primary lesion the regional lymph glands are infected, completing the primary complex. This may heal, be encapsulated and calcify. On the other hand, the primary lesion may be progressive, extending into the adjoining lung tissue; this happens often in infancy.

The great frequency of tubercle bacilli in infants is due to the fact that these children are admitted to the hospital before the tuberculous process in the lungs has had time to heal and be encapsulated, or—in

many cases—while this process is progressing into the surrounding pulmonary tissue.

In the second, third and fourth years of life the finding of tubercle bacilli is not so frequent by far. The primary lesion has had more time to heal; besides, it is not so apt to be progressive as in the first year of life and has a greater tendency to heal. Children over 4 years of age are even less apt to show tubercle bacilli. At this age, healing and encapsulation occur more readily, and it is only a matter of chance if examination for bacilli is performed when the process is fresh.

Analysis of the 199 cases in which tubercle bacilli were demonstrated by lavage shows that in no instance was the examination followed by serious inconvenience, and neither aspiration pneumonia nor aggravation of the tuberculous condition resulted. That the performance of the lavage in itself is disagreeable to the children is true,

TABLE 2.—*Positive Results According to Number of Lavages*

Age	Number of Children	Number of Lavages				
		One	Two	Three	Four	Five
0-1	54	42 (78%)	48 (89%)	51 (94%)	53 (98%)	54 (100%)
1	50	35 (70%)	43 (86%)	49 (98%)	49 (98%)	50
2	38	28 (74%)	35 (92%)	36 (95%)	37 (97%)	38
3	18	14 (78%)	18(100%)	18(100%)	18(100%)	18
4	7	6	6	7	7	7
5	11	10	11	11	11	11
6	5	3	4	5	5	5
7	8	7	8	8	8	8
8	3	2	3	3	3	3
9	3	3	3	3	3	3
10	2	2	2	2	2	2
Total	199	152 (77%)	181 (91%)	193 (96%)	196 (98%)	199 (100%)

especially when they are old enough to remember it from one time to another: in infants it is easily accomplished.

It would be an advantage to the patient as well as to the examiner if one lavage of the stomach were sufficient to determine whether or not bacilli were present. That one lavage is not enough, however, is unfortunately evident from table 2.

The presence of tubercle bacilli was demonstrated by the first lavage in 152 children, or 77 per cent; the second lavage increased the percentage to 91, and the third lavage to 96. On the fourth and fifth lavages the increase in the percentage is so slight that it seems warrantable to limit the number of examinations to three; if these give negative results, there is little chance of finding bacilli on the fourth or fifth examination.

It may be appropriate to point out once more that many of the specimens were obtained from lavage on two days in succession, the specimens being placed together for examination.

It is also to be emphasized that in the 423 children in whom no tubercle bacilli were found the examination was limited to one lavage in about half of the cases. In our opinion, therefore, these children were not examined sufficiently. Additional lavages would undoubtedly have disclosed the presence of tubercle bacilli in several cases listed as negative.

From these results there can be no doubt that this method of examination is suitable for the demonstration of tubercle bacilli in children at an age when it is difficult, and in most cases impossible, to obtain any expectoration for examination. Our experiences are in harmony with those of investigators in other countries where these examinations have been made in recent years; among others, we refer to Armand-Delille,[4] Vibert [5] and Chantegreil [6] of France, Boer [7] of Holland, Jachnis and Zilber [8] of Russia, Saye [5] of Spain, Jundell,[9] Wallgren [10] and Philipson [11] of Sweden, Baumann [12] and Opitz [13] of Germany, Schelton [5] of Cuba and Cantonnet Blanch [14] of Uruguay.

As to the technic opinions differ. Armand-Delille makes only a microscopic examination of the hemogenized sediment. He has had surprisingly good results. In a series of more than 500 cases, he found tubercle bacilli in 100 per cent of the patients who showed both auscultatory and roentgenographic signs of caseous processes in the lungs and in 60 per cent of those in whom roentgen examination furnished the only evidence of tuberculosis. Baumann, Opitz, Jachnis and Zilber and Wallgren combine microscopic examination of the sediment obtained by lavage with inoculation of guinea-pigs.

What significance may be attached to the finding of tubercle bacilli in the material obtained on lavage? Is it not conceivable that the tubercle bacilli which can be demonstrated only by inoculation of animals and by special methods of cultivation are chance visitors in the fauces and the stomach in children who do not have tuberculosis just as diphtheria bacilli, meningococci and pneumococci may be found in the throat of healthy persons?

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4. Armand-Delille: Paris méd. **1**:18, 1931.
5. Quoted by Armand-Delille.[4]
6. Chantegreil: Rev. de phtisiol.-méd.-sociale **13**:32, 1932.
7. Boer: Maandschr. v. Kindergeneesk. **1**:377, 1932.
8. Jachnis and Zilber: Zentralbl. f. d. ges. Kinderh. **25**:320.
9. Jundell: Acta pædiat. **12**:73, 1931.
10. Wallgren, A.: Tubercle Bacilli in Children with Erythema Nodosum, Am. J. Dis. Child. **41**:816 (April) 1931.
11. Philipson: Acta pædiat. **13**:393, 1932.
12. Baumann: Beitr. z. Klin. d. Tuberc. **79**:717, 1932.
13. Opitz: Acta pædiat. **11**:186, 1930; Med. Welt **5**:1239, 1931; München. med. Wchnschr. **78**:949, 1931.
14. Cantonnet Blanch: Zentralbl. f. d. ges. Kinderh. **25**:688, 1932.

To rule out this possibility we examined the sediment obtained by lavage from 158 children with negative reactions to tuberculin. About half of them were given lavage twice but tubercle bacilli were not found in a single instance. This is not a large control material, but the results are not without significance.

If, on the other hand, we take for granted that the finding of tubercle bacilli by lavage is pathologic, what significance has this for diagnosis, prognosis and therapy? Do these cases involve a risk of infections? These questions will be answered as far as practicable with the material presented.

DIAGNOSIS

When lavage shows the presence of tubercle bacilli, the child almost certainly has tuberculosis, and if it can be established that the bacilli

TABLE 3.—*Auscultatory and Roentgen Findings in Children with Tubercle Bacilli in the Lavage*

Age	Number of Children	+R* +A†	+R −A	−R −A	−A‡	+A‡
0-1	54	35	7	8	4	0
1	50	20	14	12	4	0
2	38	15	14	6	3	0
3	18	10	4	2	2	0
4	7	4	2	1	0	0
5	11	8	1	1	0	1
6	5	4	1	0	0	0
7	8	7	0	1	0	0
8	3	1	2	0	0	0
9	3	3	0	0	0	0
10	2	1	1	0	0	0
Total	199	108	46	31	13	1

* R, roentgen evidence of tuberculosis.
† A, auscultatory signs of tuberculosis.
‡ No roentgen examination.

do not originate in the fauces (tonsils, adenoids) the tuberculous process must be located in the lungs.

One may ask, however, if it is not possible, with all the other diagnostic means at one's disposal, especially auscultation and roentgenology, to make the diagnosis of pulmonary tuberculosis without the demonstration of tubercle bacilli. This may be done in many cases. In not a few cases, however, this does not hold good, as is evident in table 3 in which are recorded the auscultatory and roentgenologic findings in the 199 cases showing tubercle bacilli on lavage.

As will be noticed, we demonstrated the presence of tubercle bacilli in 46 cases in which the roentgenograms showed infiltrative processes in the lungs while no changes could be made out on auscultation, and also in 31 cases in which there were no signs—roentgen or auscultatory —of pulmonary tuberculosis. In the latter group the diagnosis of pulmonary tuberculosis could be made only on the basis of the finding of tubercle bacilli.

Similar observations have been reported by others. As already mentioned, Armand-Delille found tubercle bacilli in 60 per cent of cases in which auscultation showed no changes, the roentgen findings alone indicating a probable diagnosis of pulmonary tuberculosis. In addition, he found tubercle bacilli in some cases (the number was not given) without auscultatory or roentgen evidence of pulmonary tuberculosis.

Opitz demonstrated by lavage the presence of tubercle bacilli in cases in which the roentgenograms showed an increase in the density of the hilar shadow or an increase in the size of the hilar glands while no abnormality was revealed by auscultation.

Philipson and Wallgren found tubercle bacilli in the material obtained by lavage from 47 of 96 children (about 50 per cent) with erythema nodosum. In these cases the roentgenographic changes were limited to the hilus, and were described as slight, moderate and marked.

Baumann emphasized the significance of the demonstration of tubercle bacilli in the lavage in cases in which the increase of the hilar shadow might otherwise be more suggestive of the diagnosis of tuberculosis of the bronchial lymph glands.

Ligner [15] reported an interesting case from Gothenburg which showed that with this method of examination a condition of pulmonary tuberculosis may be diagnosed even in the preallergic stage. The patient was a child, 7 months old, whose mother was suffering from pulmonary tuberculosis. Because of the danger of infection, the child was moved from its home, although it was apparently in good health. The tuberculin tests proved negative, and roentgen examination and auscultation revealed no abnormalities. On June 6, gastric lavage showed tubercle bacilli; on June 14, the child had fever; one June 18, the Mantoux test (0.1 mg.) was positive.

We know of two similar cases which have not yet been reported.

THERAPY

The finding of tubercle bacilli in a child with a positive tuberculin reaction indicates that one is dealing with a case of tuberculosis in which the tuberculous process is not healed; that is, the patient has to be treated by every means available. In this way therapeutic measures may be instituted when the child would have recovered without treatment. Undoubtedly this happens to a great many children with tuberculous infection, but it cannot be helped. It is impossible, a priori, to decide whether the child one is dealing with belongs to this fortunate category, or whether the tuberculous infection will take a serious course.

How to deal with the child with a positive tuberculin reaction in whom the presence of tubercle bacilli cannot be demonstrated is quite a different matter. The age, the general health and the social condition

15. Ligner: Ztschr. f. Kinderh. **50**:505, 1930.

of the child are factors to be taken into consideration. Once the presence of tubercle bacilli has been demonstrated, however, the child must be under medical observation and treatment.

Moreover, gastric lavage furnishes the most reliable indication as to how long the treatment is to be continued. As long as the lavage shows tubercle bacilli the process in the lungs has not healed.

Whether the illness of the child diminishes or is aggravated is to be estimated chiefly from his general condition. In most cases auscultation, roentgen examination, the temperature chart, weight, etc., will give all the evidence required for judging the patient's condition. But the most decisive proof as to the complete healing or persistence of the process is obtained by bacteriologic examination.

Even though auscultation shows normal conditions, the roentgenograms no longer reveal infiltration, and the child is free from fever and looks well, the discharge of tubercle bacilli may go on—in some cases for a long time. Opitz has made similar observations.

TABLE 4.—*Duration of Discharge of Tubercle Bacilli*

Age	4 Mos.	5 Mos.	6 Mos.	7-9 Mos.	10-12 Mos.	1-1½ Yrs.	1½-2 Yrs.
0-1	1	1	2	2	1	2	..
1	2	..	4	5	2	1	1
2	2	1	..	1	2	..	..
3	..	..	1	1	..	1	..
Total	5	2	7	9	5	4	1

As it is of the greatest interest to learn how long the discharge of tubercle bacilli may continue—in other words, how long the treatment should be kept up—in collaboration with Oldenburg (chief physician in the Christmas Seal Sanatorium, Kolding Fiord) we examined the material obtained by gastric lavage of a number of children at intervals of one or two months until two successive examinations gave negative results (table 4).

Twenty-six children discharged tubercle bacilli for more than half a year, and 5 children discharged bacilli for more than a year.

Often the bacilli are found in only one or two specimens, and not subsequently. Still, not infrequently, bacilli are demonstrated by lavage for a long time, as is evident from the relatively large number of instances of a protracted discharge of bacilli that we have recorded during this study.

One might be inclined to think that the protracted discharge of tubercle bacilli is relatively most frequent among the children who are seriously ill, but this is far from being the case. Of the 33 children cited in table 4, only 2 died, while 25 are apparently well, 4 show considerable improvement, and 2 are yet in the sanatorium.

PROGNOSIS

Is the demonstration of tubercle bacilli of any prognostic significance? To answer this question we tried to obtain information concerning the subsequent fate of the 622 children in this series, and in a great majority of the cases were successful.

Table 5 gives the data on the 199 children in whom tubercle bacilli were found; 44 of these died, and 148 are alive; information is lacking in seven cases.

TABLE 5.—*Data on Survival of Group Showing Tubercle Bacilli*

Age	Number of Children	Condition Unknown	Alive	Dead*
0-1	54	2	29	23†
1	50	3	35	12‡
2	38	1	35	2
3	18	0	16	2
4	7	0	7	0
5	11	0	9	2
6	5	0	3	2
7	8	0	8	0
8	3	0	3	0
9	3	0	2	1
10	2	1	1	0
Total	199	7	148	44

* Death was caused by tuberculosis, except as otherwise stated.
† One died of burns.
‡ One died of burns; one of diphtheria.

TABLE 6.—*Data on Survival of Group of Children in Whom Tubercle Bacilli Were Not Found*

Age	Number of Children	Condition Unknown	Alive	Dead*
0-1	8	0	6	2†
1	58	5	45	8†
2	81	11	67	3
3	76	8	64	4
4	49	4	43	2
5	33	3	29	1
6	26	3	23	..
7	37	3	34	..
8	27	6	20	1
9	18	1	17	..
10	10	2	8	..
Total	423	46	356	21

* Death was caused by tuberculosis, except as otherwise stated.
† One died of pneumonia.

Taking separately the children in the first four years of life, we lack information concerning 6 of this group. Of the remaining 154 children, 39 died (i. e., 25.3 per cent). For all the children up to 10 years of age the mortality percentage is 22.9.

Table 6 comprises the children in whom the presence of tubercle bacilli was not demonstrated—a total of 423. There is no information concerning 46. Of the others, 21 died, while 356 are alive. In this group the mortality percentage for the 4 youngest age-groups is 8.5; for all the children up to 10 years of age it is 5.5.

Of course, a larger series would have been most desirable for consideration of the prognosis. Judging from these figures, however, the prognosis is most unfavorable for the children in whom tubercle bacilli are found. Thus, one fourth of the children under 4 years of age yielding tubercle bacilli died and only one twelfth of those in whom examination gave negative results. Of all the children from whom our material was obtained, about one fifth of those showing tubercle bacilli and only about one twentieth of those in whom bacilli were not found died.

While it was not difficult to obtain information about the subsequent fate of the patients as far as life and death were concerned, it was by no means easy to secure reliable information as to the condition of the children who were still alive. We tried as far as possible to have the children examined by us or by other physicians, but in most cases we had to be contented with the parents' judgment; naturally this is to be accepted only with a great deal of caution. The statement that the child spends a few months, year after year, in a seashore sanatorium may mean that it is really ill; on the other hand, the child may be living under such unfavorable social conditions that the physician tries to protect it from infection by having it admitted to the sanatorium; or, the parents, merely for the sake of profit, may secure for their child a stay in the country, free of charge.

Nor is much significance to be attached to the statement that the child often has fever, that it is losing weight and that its appetite is poor; these symptoms may be due to many other diseases besides tuberculosis. On the other hand, when the parents think that the child is well, this is not necessarily true. Even when an examination is performed by a physician it is difficult to judge the condition of the lungs without roentgen and other examinations, especially if the child happens to have an attack of ordinary acute catarrhal bronchitis.

Therefore, whenever it has been practicable we have had the children admitted to the hospital for a thorough examination when their condition has been doubtful.

In tables 7 and 8 we have recorded, as objectively as possible, all the information obtained. Of the 148 surviving children who showed tubercle bacilli 85.8 per cent were found to be well after an observation period averaging two years. Of the 356 surviving children in whom examination gave negative results, 85.9 per cent were well after the same period.

If any conclusion is to be drawn from these tables, it is that most of the children who do not succumb rapidly to the tuberculous infection are well after an average observation period of two years, and that in this respect there is no difference between children who do, and those who do not, show the presence of tubercle bacilli.

DANGER OF INFECTION

A priori, it would seem that children with active pulmonary tuberculosis are as likely to communicate the infection as are adults with tubercle bacilli in their expectoration. In fact, in previous papers we have held this to be an incontestable fact, and have consequently insisted on thorough measures of isolation in all hospital and convalescent homes in which these patients are treated together with non-

TABLE 7.—*Condition of the Children in Whom Tubercle Bacilli Were Found*

Age	Number of Children	Well	Improved	Ill	In Sanatorium	Dead	Observation Period for Surviving Children			
							1 Yr.	2 Yrs.	3 Yrs.	4 Yrs.
0-1	52	21	4	..	4	23	4	10	10	1
1	47	31	2	..	2	12	9	20	3	1
2	37	32	1	..	2	2	7	16	9	1
3	18	15	1	..	..	2	4	9	3	..
4	7	5	..	..	2	..	..	3	2	..
5	11	7	..	1	1	2	2	3	3	..
6	5	3	..	..	..	2	..	..	2	1
7	8	7	1	..	..	..	1	4	3	..
8	3	3	..	..	..	..	1	2	..	..
9	3	2	..	..	..	1	..	2	..	..
10	1	1	..	..	..	..	..	1	..	..
Total	192	127	9	1	11	44	28	70	35	4

TABLE 8.—*Condition of the Children in Whom Tubercle Bacilli Were Not Found*

Age	Number of Children	Well	Improved	Ill	In Sanatorium	Dead	Observation Period for Surviving Children			
							1 Yr.	2 Yrs.	3 Yrs.	4 Yrs.
0-1	8	4	..	..	2	2	2	2	..	..
1	53	39	1	..	5	8	8	25	4	3
2	70	60	5	..	2	3	11	44	9	1
3	68	56	6	..	2	4	10	33	17	2
4	45	40	3	..	..	2	4	26	11	2
5	30	23	1	..	5	1	3	12	9	0
6	23	18	2	..	3	..	1	10	9	..
7	34	25	4	..	5	..	8	16	5	..
8	21	19	1	..	..	1	1	11	5	3
9	17	15	1	..	1	..	4	9	2	1
10	8	7	..	1	..	..	2	5	1	..
Total	377	306	24	1	25	21	54	193	72	12

tuberculous children; further, as so many children under 4 years of age with positive tuberculin reactions are discharging bacilli, it has been our view that these measures of isolation ought to apply to all children of this age with positive tuberculin reactions until a reasonable observation period and thorough examination (including three examinations of the material obtained by gastric lavage) have shown whether or not there is danger of infection.

On the other hand, we have not had any scruples about having children over 4 years of age with a positive tuberculin reaction in the same wards as those with a negative reaction, unless the former pre-

sented symptoms of active tuberculosis, such as pleurisy, pulmonary tuberculosis and erythema nodosum.

Opinions differ, however, and as the whole question seems to be most important, we think it appropriate to review the literature on this particular point.

Baumann (Kinderklinik der Universität Basel) said that in infancy even a small number of tubercle bacilli—demonstrable only on inoculation of animals—may be dangerous to persons in the patient's environment. It is true that, as a rule, this does not apply, to the older members of the family in the home of the child, but in day nurseries, asylums and similar places even the small numbers of tubercle bacilli discharged by an infant may be dangerous for other small children. It is only proper, therefore, to insist that every new patient be tested with tuberculin, and if the test is positive, the child must be examined thoroughly in order to ascertain the character of the tuberculous process.

It cannot be proved indisputably that infants and small children with open tuberculosis are not likely, under the aforementioned conditions, to communicate the infection to others. We know with certainty only that wherever bacilli are discharged by coughing there is a possibility of infection. Therefore, demonstration of tubercle bacilli in children of this age by inoculation of animals is not only of scientific interest but also of practical significance.

In Baumann's series tubercle bacilli were demonstrated in 29 children between 4 and 15 years of age, and in 23 of these the presence of tubercle bacilli was ascertained only by animal experiments. Baumann said that the fact that such cases of open tuberculosis are a source of great danger to other children is well known. He cited two instances to illustrate the havoc that may be inflicted on infants and small children by unnoticed cases of open pulmonary tuberculosis. It is true that in these two instances the source of infection was not in other children but in parents whose sputum contained tubercle bacilli, although microscopic examination had repeatedly given negative results.

Cases of this kind are far from infrequent. Much more often than was formerly believed the adult patient with "abacillary" consumption proves to be discharging tubercle bacilli; the bacilli are not found on microscopic examination of the expectoration, but their presence is demonstrated by animal experiments or by cultivation.

Clausen [16] examined in this way the material obtained by gastric lavage from 38 adults with consumption in whom he had not been able to find tubercle bacilli by the usual methods; the result was that 20 were found to be discharging bacilli.

16. Clausen, V.: Acta tuberc. Scandinav. **5**:379, 1931.

Heimbeck,[17] of Norway, holds that tuberculous children in the first three years of life are to be regarded as likely to communicate the infection until it is proved that they do not, and that such children are therefore to be isolated from those with negative tuberculin reactions. He further thinks that children who are exposed to tuberclosis, and who hence must be removed from their homes, should be divided into two groups, those with a positive and those with a negative tuberculin test, and that these groups should be kept separate.

Wallgren concluded from his examination of children with erythema nodosum by means of gastric lavage that these patients are carriers of tuberculous infection, that they must therefore not be allowed to attend school until some time after the onset of the disease, and that they should be isolated when they are admitted to a hospital.

At the International Congress of Pediatrics in Stockholm in 1930, Monrad stated that the first and second lavages not infrequently showed tubercle bacilli; and that the presence of the bacilli on the third lavage was demonstrated only by animal experiments. He did not think such children so likely to communicate the infection that they must be isolated *at any cost.*[18] We have several cases of this kind in our material and in the German literature they were mentioned by Baumann and by Opitz as "veiled" (*verkappte*) carriers of tubercle bacilli.

Opitz (Kinderklinik der Universität Berlin) said that the frequent demonstration of tubercle bacilli in children is in many respects surprising and perhaps alarming. Its practical importance cannot be estimated at present. It is far from desirable to produce a general tubercle-bacillophobia; on the other hand, this source of infection is to be reckoned with in children's hospitals, asylums and similar institutions. Since there is danger of superinfection, it is not justifiable to have the veiled carriers together with children with open tuberculosis, and of course it would not be justifiable to place them in the same ward as children with negative tuberculin reactions.

Children who discharge tubercle bacilli, even though this can be demonstrated only by animal experiments, should at least be barred from schools.

As Opitz further pointed out, it would be wrong to overlook this observation on the supposition that the danger of infection cannot be great, as there are evidently only small numbers of tubercle bacilli present.

How many or how few bacilli it takes to produce tuberculosis we do not know with certainty. Besides other factors, infection depends also on the virulence of the bacilli and on the susceptibility of the person

17. Heimbeck: Acta pædiat. **12**:70, 1931.

18. Italics by the authors.

exposed to them. It is known that children, especially infants, are very susceptible to tuberculous infection.

The virulence of the tubercle bacilli found on lavage and their number (many or few) are points that must be settled before it is possible to know whether there is danger of infection. The reader is referred to the work of Lester [18a] on the estimation of the virulence and number of tubercle bacilli obtained on gastric lavage.

Even though it is only reasonable to admit that an infant who spends all its time in bed is less likely to communicate infection than is an adult who is walking about, expectorating bacilli by the thousands, we are convinced—from the investigations carried out by Lester—that children who are discharging tubercle bacilli communicate this infection, and that it would be wrong to consider that they do not.

TABLE 9.—*Results of Examination of Material Obtained by Gastric Lavage for Tubercle Bacilli in the Finsen Light Institute* *

Age	Number of Children	Positive	Negative
0-1	1	1	0
1	2	2	0
2	5	3	2
3	1	0	1
4	5	1	4
5	3	0	3
6	2	0	2
7	2	0	2
8	1	0	1
9	2	0	2
10	0	0	0
Total	24	7	17

* Data furnished by O. Chievitz.

Certainly, the danger of infection is greatest in the cases in which extensive processes can be demonstrated in the lungs by auscultation or by roentgen examination, and least when no sign of tuberculosis is revealed by auscultation or roentgenography while the presence of bacilli is ascertained only after repeated lavages. In our opinion, the possibility of infection is present also in the latter cases, and it has to be taken into consideration in placing such patients among other children.

Do children with surgical, nondischarging, tuberculosis constitute a source of infection? This depends on the condition of the lungs. Such diseases as spondylitis, coxitis, spina ventosa and tuberculous epididymitis originate, as a rule, secondarily from a tuberculous focus in the lungs. If the focus in the lungs has healed when the surgical lesion is treated, there is no danger of infection. If, on the other hand, the focus in the lungs has not healed, there is still a possibility that the infection may be communicated to others. Before it can be determined

18a. Lester, V.: Four Years' Experience with Examination of Material Obtained by Gastric Lavage, Am. J. Dis. Child., this issue, p. 322.

decisively that the lesions are healed, the lungs must be examined thoroughly, and the physical examination should include gastric lavage.

In the children with surgical tuberculosis under treatment in the surgical department of the Finsen Light Institute (table 9) gastric lavage showed tubercle bacilli in 7 of 24 children, that is, in about one third, which is a large proportion. From these findings it looks as if such patients are likely to convey the infection to others. But turning to the investigations carried out by Dorph-Petersen [19] in the seashore hospital at Refsnæs, we arrive at the opposite conclusion. In this group of 72 children with surgical tuberculosis, gastric lavage showed tubercle bacilli in only 1 patient, a girl of 13 years, in whom no other sign of an active tuberculous process in the lungs could be demonstrated, either by auscultation or by roentgen examination.

The difference between the results of these two series of investigations is readily explained, however. In the Finsen Institute 6 of the children were less than 3 years old, and they all showed tubercle bacilli, whereas in the hospital at Refsnæs the great majority of the children were over 7 years (only 3 were between 2 and 3 years of age, and none was younger).

Thus, as far as the discharge of tubercle bacilli from the lungs is concerned, children with surgical tuberculosis appear to behave like children in whom the tuberculosis is localized entirely in the lungs; the smaller the children are, the greater is the probability that the pulmonary disease has not yet healed, and that tubercle bacilli are therefore discharged.

THEORETICAL CONSIDERATIONS

In the preceding paragraphs we have dealt almost exclusively with the practical significance of gastric lavage in diagnosis, prognosis, therapy and epidemiology. However, the surprisingly frequent finding of tubercle bacilli in small children also gives rise to theoretical considerations; it shows with a probability which approaches certainty that tuberculosis of the bronchial and hilar glands never occurs alone, but is always associated with a tuberculous process in the lungs.

In our opinion, the lungs constitute the first site of attack, and the regional lymph glands are infected from this primary focus, so that at some time both the glands and the lungs are sites of tuberculosis. The pulmonary tuberculosis may clear up before the glandular tuberculosis does, so that there is a period in which tuberculosis of the bronchial lymph glands is associated with healed tuberculosis of the lungs.

As long as the process in the lung has not healed it is possible at some time to demonstrate the presence of tubercle bacilli in the material

19. Dorph-Petersen: Ugesk. f. læger **94**:412, 1932.

obtained by gastric lavage from a child with a positive tuberculin reaction. Exceptions to this rule are the relatively rare cases of primary tuberculosis of the intestines or of some other part of the body.

That the development of the tuberculous process may take the reverse course—a primary site in the lymph glands at the hilus and subsequent extension of the infection to the lungs—seems altogether improbable. Indeed, it would be contrary to all other observations on the extension of infection; everywhere in the body, an organ or an area of the skin is first attacked by the infection and then the regional lymph glands.

The diagnosis "tuberculosis of the bronchial lymph nodes" should be discarded, at least as the main diagnosis. In all probability the condition never exists except in association with healed or active pulmonary tuberculosis.

That roentgenograms often show only enlargement of the hilar shadows and no infiltrative processes in the lungs does not mean that the lungs are not attacked by tuberculosis. The investigations reported by Baumann, Opitz, Wallgren and us have established the fact that in many such cases (in about one half of those in Wallgren's series) there is, in addition, an open process of pulmonary tuberculosis.

FOUR YEARS' EXPERIENCE WITH EXAMINATION OF MATERIAL OBTAINED BY GASTRIC LAVAGE

II. DEMONSTRATION OF TUBERCLE BACILLI

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During the past few years examination of the stomach contents for tubercle bacilli has gained more and more favor as one of the tests which in case of doubt may help the clinician in the diagnosis of pulmonary tuberculosis. The clinical value of the method has been elucidated by Poulsen [1] in regard to children and by Clausen [2] in regard to adults.

Another point of importance, to which attention has been drawn by Poulsen, is the danger of infection presented by these patients. Hitherto this has been taken up only on a clinico-epidemiologic basis. It was therefore considered warranted to publish an account of the danger from a purely bacteriologic point of view.

Consequently, in this part of the work a description will be given of the technical basis on which these investigations rest. In addition I shall consider the danger of infection, based partly on determinations of the virulence of strains isolated from the stomach contents and partly on investigations of the number of tubercle bacilli grown from each sample.

The bacteriologic tests were made in the tuberculosis department of the State Serum Institute.

TECHNIC

The same technic has not been employed throughout the investigations, which began in 1928, but it has been subjected to various alterations as experience dictated, one of the most important of these being the change from Petroff's to Löwenstein's medium. The preparation of these mediums and the procedure employed have been described by Kristensen and Jensen.[3]

From the State Serum Institute; Chief, Dr. T. Madsen.

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1. Poulsen, V., and Andersen, A. O.: Four Years' Experience with Examination of Material Obtained by Gastric Lavage: I. Demonstration of Tubercle Bacilli and Its Significance in Prognosis, Therapy and Estimation of Danger of Infection, Am. J. Dis. Child., this issue, p. 307.

2. Clausen, Vilhelm: Über Die Bedeutung der Magenspulwasseruntersuchung für die Diagnostik der Lungentuberculose, Acta tuberc. Scandinav. **5**:379, 1931.

3. Kristensen, Martin, and Jensen, K. A.: Hospitalstid. **67**:241, 1924; Compt. rend. Soc. de biol. **90**:45, 1924. Jensen, K. A.: Zentralbl. f. Bakt. (Abt. 1) **125**: 222, 1932.

Whereas formerly cultivation failed in as many as from 25 to 30 per cent of cases which gave positive results in the inoculation of guinea-pigs, by the methods now employed positive cultures are obtained in 100 per cent, and it has been found possible to do without experiments on animals in all cases other than those of children under 5 years of age.

The method employed is as follows:

From 200 to 300 cc. of the material obtained by gastric lavage is allowed to stand from eighteen to twenty-four hours, after which the sediment is sent to the Institute (in the area around Copenhagen, however, the entire quantity of liquid is usually sent in). It is centrifugated, and smears are made for microscopic examination. The remainder is divided into two portions, one of which is homogenized with 4 per cent sodium hydroxide; the other, with 6 per cent of sulphuric acid by volume.

The soda homogenization proceeds at 37 C. for about twenty minutes, the glass being shaken now and then. After centrifugation at high speed for twenty minutes the supernatant fluid is removed, and the sediment is neutralized with 2 drops of 8 per cent hydrochloric acid; half of this is seeded with a Pasteur pipet in three Löwenstein tubes. The rest, together with some of the acid-homogenized material, is inoculated, partly subcutaneously and partly intraperitoneally, into a guinea-pig. For the acid homogenization about 5 cc. of 6 per cent sulphuric acid is added, and the sample after vigorous shaking is allowed to stand in darkness for five minutes at room temperature. After the addition of from 10 to 15 cc. of saline solution and brief centrifugation, the rather voluminous sediment is seeded in three tubes with a platinum loop. The rest is mixed with the part of the soda-homogenized portion that is intended for the inoculation of guinea-pigs. In all cases in which there is sufficient sediment to permit of division, this technic is now used as a matter of routine, as it has been found that some strains best withstand the acid homogenization, whereas others give better results with soda homogenization. Thus parallel utilization of both methods should offer the best chance of obtaining positive results.

The tubes are sealed with paraffin, incubated at 38 C. and examined once a week. As soon as a culture is found to be positive, generally after from eighteen to twenty-five days, a smear is made for microscopic confirmation. The one who has sent the specimen is then notified to this effect, and the culture is put aside for subsequent counting of colonies and perhaps determination of type. If there is no growth after six weeks, the results of cultivation are considered negative, and the doctor who has sent the culture notified. The tubes are observed, however, for another four weeks, as a few colonies grow as late as this.

In the inoculation of guinea-pigs rather weak reactions were sometimes obtained. In some cases tuberculosis developed only following subcutaneous inoculation; in others, only following intraperitoneal inoculation. This is probably due to the fact that the conditions under which the tubercle bacilli multiply are different. With intraperitoneal inoculation there is the possibility not only of spread over a large surface, but also of a rapid and powerful reaction of the entire body. With a subcutaneous injection a less widespread, better protected focus is first obtained, from which the bacteria later spread over the whole body.

In earlier experiments unhomogenized material was used for the inoculation of guinea-pigs, as experience with tests of the urine had indicated that even the most careful homogenization may destroy the tubercle bacilli. This procedure was abandoned, however, as a large number of the guinea-pigs died of infection from other bacteria, even when they had been inoculated solely by the subcutaneous method.

The tests on guinea-pigs were concluded after six weeks. At autopsy one cannot always find a typical general tuberculosis. In some cases there is only a slight enlargement of the regional glands, i. e., the inguinal or lumbar glands, corresponding to the site of the subcutaneous injection, and of a small gland near the pylorus, as well as a somewhat larger gland in the porta hepatis, which shows that the intraperitoneal injection has taken effect. Microscopic examination of these glands reveals numerous tubercle bacilli which, on reinjection into guinea-pigs, produce general tuberculosis; likewise, the injection of some of the culture from the mediums inoculated always gives rise to general tuberculosis in the guinea-pig. Thus the phenomena described have nothing in common with the question of an ultravirus.

VIRULENCE AND QUANTITY OF BACTERIA

During a period of eighteen months—from November, 1930, to April, 1932—by the use of this technic tubercle bacilli were demonstrated in the material obtained by gastric lavage from 260 patients. In some cases several samples were sent in—up to 12 per patient—making 513 in all, and of these 380 gave positive results. On the basis of this material, by means of a series of experiments and also by arranging the results in tables, an endeavor has been made to throw light on the following problems: first, the virulence of these bacteria; second, the "bacteriologic" infectivity of patients with tubercle bacilli in the gastric contents.

To form an idea of the virulence of the tubercle bacilli found, the results of inoculation of guinea-pigs and of planting on mediums were grouped as shown in table 1.

The second column in table 1 shows that most of the strains of bacilli produced both growth on a medium and a positive reaction in guinea-pigs. The third column shows the cultures that gave growth but a negative reaction in guinea-pigs; the size of this group—about one fifth of all the strains giving positive reactions—raises the question whether these bacteria were at all virulent for guinea-pigs, or whether they were tubercle bacilli at all.

To settle the question subcultures were made of practically all the strains, and 1 mg. was injected subcutaneously into guinea-pigs. After six weeks the animals all showed well developed general tuber-

culosis. Thus these strains, when inoculated in suitable doses, produced characteristic tuberculous changes in guinea-pigs, while the cultures all showed the characteristics of the human type of tubercle bacilli. Consequently, the more probable explanation of the failure of the primary guinea-pig test is that these samples contained only a few bacteria able to multiply. As a matter of fact, a more careful examination of this group showed that most of the specimens yielded only sparse growth; 44 of the 56 cultures showed only from 1 to 3 colonies, 10 cultures between 4 and 9 colonies and only 2 cultures a larger number.

For purposes of comparison it might be added that in the group that gave both growth and positive reactions in guinea-pigs, 57 specimens

TABLE 1.—*Results of Culture and Inoculation*

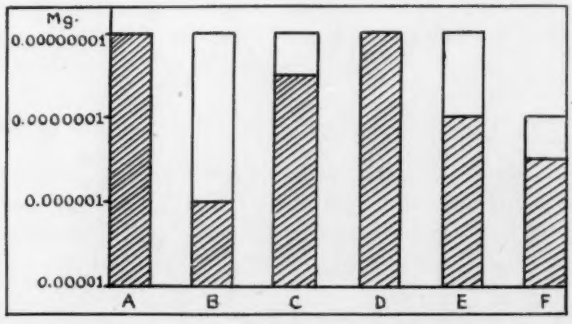
Age of Patient	+ Growth + Guinea-Pig		+ Growth 0 Guinea-Pig		0 Growth + Guinea-Pig	
0 to 1	64.7%	37	15.9%	7 (13%)	19.4%	12 (21%)
1 to 2		38		8 (14%)		10 (18%)
2 to 3		22		6 (14%)		6 (18%)
3 to 4		13		6 (25%)		5 (20%)
4 to 5	70.4%	6	25.9%	3 (30%)	3.7%	1 (10%)
5 to 10		17		6 (26%)		0
10 to 15		5		5 (45%)		1 (10%)
15 to 20		17		3 (14%)		1 (5%)
20 to 30		26		5 (16%)		0
>30		5		6 (50%)		1 (9%)
Total		186		56		37

yielded from 1 to 3 colonies, 63 specimens from 3 to 20 colonies and 66 specimens 20 colonies. It is not easy to decide whether the specimens originally contained only a few bacteria, or whether actually there were a large number, which were attenuated or killed by their sojourn in the stomach and later in the wash water. My experience rather seems to support the latter theory, as in some cases acid-fast and alcohol-fast rods were found in the smears in cases in which the guinea-pig test as well as cultures later gave a negative result and as in other cases the cultures failed to show as many colonies as one might expect from microscopic examination of the sample. That in such cases it is only a passing attenuation is shown by the aforesaid experiments with inoculation.

To study this question more profoundly, further tests of virulence were performed with 6 selected cultures: 4 strains isolated from the gastric contents and 2 strains from the spinal fluid.

The cultures were selected as follows: Two (A and B) were from specimens that had given a positive culture but a negative reaction in guinea-pigs, 2 (C and D) from specimens with which a positive culture and general tuberculosis in guinea-pigs were obtained, and 2 (E and F) from spinal fluid which gave growth and a reaction in guinea-pigs. Each culture was injected in decreasing doses from 0.1 to 0.00000001 mg.; two guinea-pigs were used for each dose, one being killed after six weeks and the other after three months. At the same time Löwenstein's medium and Besredka's fluid egg medium were inoculated.

The accompanying diagram is a schematic illustration of the results. The shaded portions of the columns indicate the doses that caused both growth and a reaction, whereas the white portions denote doses which caused growth without a reaction, thus expressing the virulence of the cultures in the experiments on guinea-pigs.



Schematic representation of results in tests of virulence with 6 selected cultures: *A* and *B* from specimens of gastric lavage that had yielded growth but no reaction in guinea-pigs; *C* and *D* from specimens yielding both growth and a reaction, and *E* and *F* from spinal fluid giving both growth and a reaction. The vertical scale gives the dose injected. The shaded portions indicate both growth and a reaction in guinea-pigs; the white portions, growth only.

Even if the figures are too low to permit of any definite conclusions being drawn from the experiment, they indicate that there is no parallelism between the result of the primary guinea-pig test and the actual virulence of the culture, nor does there seem to be any great difference in virulence between the strains isolated from gastric contents and those cultivated from spinal fluid.

Comparison of this diagram with the figures in column 3 of table 1, and with the foregoing observations as to the discrepancy between colony numbers or growth and the direct demonstration of tubercle bacilli, indicates that these bacteria have been exposed to some injurious influence which has caused a temporary reduction of virulence.

If one examines the last column in table 1, showing the number of specimens that produced a tuberculous lesion in guinea-pigs but did not give growth, one is struck by the fact that 33 of the 37 samples were from children under 4 years of age. I can give no real explanation of this interesting phenomenon. Two theories are suggested: 1. The tubercle bacilli are more virulent in infants. 2. The tubercle bacilli are less exposed to injury in infants than in older children and adults.

Were one to assume increased virulence, it is difficult to understand why cases in column 3 showed no virulence for guinea-pigs. One might be tempted to believe that the results in this group represent the normal, as specimens containing few bacteria give growth and infection of guinea-pigs with almost equal frequency. In routine examinations in the laboratory during the same period, however, other specimens than those secured by gastric lavage yielded a positive culture and a negative reaction in guinea-pigs 19 times and no growth and a positive reaction only 5 times. Thus there is no acceptable explanation of the results for the group less than 4 years of age.

The great difference between the results in columns 3 and 4 for the patients over 4 years of age might well be explained both by the superior results of culture over animal experiments and by some injurious action of the gastric juice on the tubercle bacilli which affects virulence rather than the ability to grow. In addition, there is a higher percentage of bacteria per sample than in infants, which may explain why so many specimens have given both reaction and growth, despite the supposed injurious influence.

As to the other main question, the danger which these patients offer to persons in their environment, one must consider two different factors: 1. How many tubercle bacilli capable of multiplying do the patients secrete? 2. What possibilities are there of their causing a spread of infection?

Whereas the second question can be answered only by means of clinico-epidemiologic research, the first may quite well be dealt with from a purely bacteriologic point of view, as one simply counts the colonies obtained from every sample. Consequently, in the 337 cases that showed growth the colonies were counted, and the figures arranged in a table according to age, separately for each year up to 5 years and thereafter by five year groups from 5 to 30. As only 19 patients over 30 years of age were investigated, they were considered in one group. The figures were further arranged according to the number of colonies: separately for each number up to 10 colonies and the remainder according to groups of 10 to 20, 20 to 70 and more than 70 colonies. Closer

examination of these figures, however, displayed such great concordance between the different subgroups that the rather ponderous tabulation was condensed into tables 2 and 3.

Table 2 shows that in the specimens there were often only a few tubercle bacilli capable of multiplying; this was especially true for the age group from 0 to 10 years, in which about half of the specimens gave growth of only from 1 to 3 colonies. In table 3 this is still more evident. The specimens yielding the small number of colonies comprised 78 per cent of those from children under 10 years of age and only about half this number of specimens from patients over 10 years. Of the other half, the greater part yielded more than 70 colonies, the

TABLE 2.—*Positive Cultures in Relation to Number of Colonies and Age of Patient*

	Number of Colonies							Total No. of Samples
	1	2	3	4-10	10-20	20-70	>70	
0 to 10 years	47 (23%)	25 (13%)	16 (8%)	52 (25%)	19 (9%)	19 (9%)	28 (13%)	206
>10 years	24 (18%)	12 (9%)	8 (6%)	16 (12%)	10 (8%)	16 (12%)	45 (35%)	131
Total	71	37	24	68	29	35	73	337

TABLE 3.—*Positive Cultures in Relation to Number of Colonies and Age of Patient*

	Number of Colonies	
	1-20	>20
0 to 10 years	159 (78%)	47 (22%)
>10 years	70 (53%)	61 (47%)
Total	229 (68%)	108 (32%)

number grown from one third of all the specimens from patients over 10 years of age. As the number of colonies in this group for the most part were close to or above the limit of the number that one can count, these must have been patients with a copious secretion of bacilli who presumably became clinically negative from swallowing their own sputum, but who, through coughing, etc., presented the same danger of infection as any patient with an open process.

On the other hand, from children under 10 years of age there were in all 28 specimens yielding more than 70 colonies, of which only 10 (from 7 patients) reached the highest values.

Bacteriologically, then, there is a great difference in the possible infectivity of these patients. While half of those over 10 years of age must be placed on a level with ordinary consumptives, only a few tubercle bacilli have been found in most of the small children, even when numerous samples have been received from the same patient

A protracted but sparse secretion of bacilli of this sort is recorded in table 4.

Nevertheless, the examples given in table 5 show that one cannot draw too far-reaching conclusions from a single sample with few or no bacteria.

As it seems to be difficult to distinguish bacteriologically between children who secrete many tubercle bacilli and those who secrete only a few, the number of bacilli recovered in both groups has been compared

TABLE 4.—*Bacteriologic Observations*

Patient	Date	Colonies per Sample
E. T., 18 months old	11/26/30	1
	12/16/30	3
	2/17/31	3
	4/14/31	3
	9/24/31	1
	12/ 3/31	0
	1/12/32	0
	2/25/32	5
	4/12/32	0

TABLE 5.—*Bacteriologic Observations*

Patient	Date	Colonies per Sample
W. L., 6 months old	1/30/31	0
	3/ 2/31	0
	5/ 5/31	0
	8/ 6/31	125
	9/26/31	0
E. I. A., 18 months old	9/ 2/31	6
	10/16/31	0
	11/27/31	227
	12/10/31	130
	2/29/32	22
	7/16/32	13
W. E., 2½ years old	3/16/31	0
	9/14/31	1
	10/16/31	1
	10/28/31	2
	11/12/31	62
	11/19/31	0
	12/10/31	0

with the data in the patients' records, with the expectation of finding that many bacilli were present in children who were clinically very ill, with pronounced stethoscopic and roentgenologic changes, and few bacilli in those who were not so ill and perhaps able to be up and about. This was only approximately the case, however, as in both groups there were exceptions. Even if these figures are too low to permit of definite conclusions, they indicate that it will always be difficult for the clinician to decide how infectious a given patient is.

SUMMARY

The bacteriologic technic for demonstrating tubercle bacilli in the gastric contents has been described. The specimens received at the State Serum Institute from November, 1930, to April, 1932—in all, 380 positive samples from 260 patients—were tested to determine both the virulence of the tubercle bacilli present and their number.

Nothing was found to indicate that these bacteria are less virulent than tubercle bacilli isolated from other parts of the human organism.

The material obtained by gastric lavage gave a growth of more than 20 colonies in 47 per cent of the adults and older children and in only 22 per cent of the patients under 10 years of age. Of the positive specimens from these children 44 per cent gave a growth of only from 1 to 3 colonies. At the present time there is no practical method of distinguishing the children who secrete many tubercle bacilli from those who secrete only a few.

With cultivation on Löwenstein's medium the percentage of growth is so high that it must be considered superfluous to inoculate guinea-pigs except when the patient is less than 5 years of age, when special circumstances seem to prevail.

CONCLUSIONS

It has been shown that children under 10 years of age secrete by no means as many tubercle bacilli as older children and adults. It must be remembered, however, that whereas samples were secured from all children with disease or suspected disease, a certain selection was made by the hospitals as to the adults, as no material obtained from gastric lavage was sent in from patients with microscopically positive expectoration. Thus a large number of the most infectious cases escaped tabulation, and there is no doubt that the difference in bacteriologic infectivity between the two age groups is still greater than appears from the tables. It remains for the clinicians to decide how great a danger these children present to persons in their environment. However, as no means are yet available for pointing out the relatively few small children who intermittently secrete many tubercle bacilli, theoretically it will be best to keep children with positive gastric contents separate from persons who presumably are especially sensitive to infection, i. e., small children, particularly those who are ill.

RELIEF OF OLIGURIA IN DEHYDRATION IN INFANTS BY INTRAVENOUS INJECTIONS OF DEXTROSE

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Investigations on dehydration accompanying infantile diarrhea during the last few years have revealed the great significance of the acidosis which is so often present. Czerny [1] was the first to call attention to this acidosis when he pointed out the similarity of the deep breathing which frequently occurs to that seen in dogs poisoned with mineral acids. Howland and Marriott [2] confirmed this observation when they found that the alveolar carbon dioxide tension and p_H of the serum of dehydrated infants were much lower than normal. Chemical examination of the blood by Schloss and Stetson [3] revealed a decreased carbon dioxide content. Later workers [4] have abundantly confirmed these reports.

There are several possible explanations for this acidosis. Czerny and Keller [5] believed that it was due to an abnormal concentration of organic acids in the blood as the result of unusual metabolism or unusual absorption from the intestines. Howland and Marriott,[2] how-

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1. Czerny, A.: Zur Kenntnis der Gastroenteritis im Säuglingsalter: IV. Respirationsstörungen, Jahrb. f. Kinderh. **45**:271, 1897.

2. Howland, J., and Marriott, W. McK.: Acidosis Occurring with Diarrhea, Am. J. Dis. Child. **11**:309 (May) 1916.

3. Schloss, O. M., and Stetson, R. E.: The Occurrence of Acidosis with Severe Diarrhea, Am. J. Dis. Child. **13**:218 (March) 1917.

4. (*a*) Hartmann, A. F.: Chemical Changes Occurring in the Body as the Result of Certain Diseases: I. The Effects of Diarrhea, Vomiting, Dehydration and Oliguria on the Acid-Base Balance of the Plasma of Infants with Mastoiditis, Am. J. Dis. Child. **35**:557 (April) 1928. (*b*) Hamilton, B.; Kajdi, L., and Meeker, D.: The Acidosis of Acute Diarrhea in Infancy, ibid. **38**:314 (Aug.) 1929. (*c*) Hoag, L. A., and Marples, E.: Acid-Base Status in Dehydration Accompanying Diarrhea in Infants: Effect of Treatment with Parenteral Fluids, ibid. **42**:291 (Aug.) 1931.

5. Czerny, A., and Keller: Jahrb. f. Kinderh. **45**:274, 1897.

ever, were unable to demonstrate any abnormal excess of acetone bodies in the blood of infants suffering from dehydration with acidosis; so they concluded that this could not be the correct explanation of the condition. Attention was then turned to the loss of base from the body by way of the voluminous fecal output. Holt, Courtney and Fales [6] in 1915 showed that large amounts of base were lost by this route. Conversion of their data to milliequivalents, however, showed that the ratio of fixed acid to base in these diarrheal stools was practically the same as in normal stools. Holt [7] has recently republished these data and added to them the analyses of the urine of the same infants (chart 1). From these figures, it may be seen that one of the principal causes of the acidosis is the disproportionately small amount of acid ions lost through the urine. The chief route of acid excretion

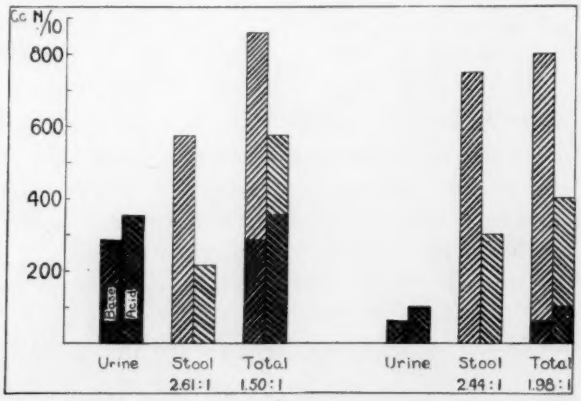

Chart 1.—The excretion of fixed base and acid in urine and stool by normal infants and by infants suffering from diarrhea (data of Holt: Am. J. Dis. Child. **39**:1346 [June] 1930). The term fixed base includes sodium, potassium, calcium and magnesium; fixed acid, chlorine and phosphorus. A valence of 1.8 was assumed in converting phosphorus to cubic centimeters of tenth-normal solution.

from the body is through the kidneys, and it has long been known [8] that the volume of urine is small in severe diarrhea. Further evidence of renal insufficiency was demonstrated by Schloss [9] in 1918, when he found

6. Holt, L. E.; Courtney, A. M., and Fales, H. L.: The Chemical Composition of Diarrheal as Compared with Normal Stools in Infants, Am. J. Dis. Child. **9**:213 (March) 1915.

7. Holt, L. E., Jr.: The Mineral Metabolism in Diarrhea, Am. J. Dis. Child. **39**:1346 (June) 1930.

8. Holt, L. E., and Howland, J.: The Diseases of Infancy and Childhood, New York, D. Appleton and Company, 1926, p. 285.

9. Schloss, O. M.: Intestinal Intoxication in Infants, Am. J. Dis. Child. **15**:165 (March) 1918.

that the concentrations of nonprotein nitrogen and urea in the blood were abnormally high in these cases.

The relief of acidosis therefore depends largely on the restoration of adequate renal function, and early treatment should be considered from this point of view. The primary aim in the treatment of dehydration has always been the replenishment of the depleted water stores of the body. Water has been administered by mouth as far as possible, but this has usually been quite inadequate and has frequently been interrupted by the occurrence of vomiting. Sodium chloride solution has been given by many routes (hypodermoclyses, intravenous and intraperitoneal injections and continuous nasal drip). This treatment provides both water and electrolytes, but, if oliguria persists, fails to ameliorate the acidosis, as Hartmann [4a] pointed out. Dextrose solution has been administered by both intravenous and intraperitoneal routes. The earlier writers stressed its value as a nutriment and a source of free water,[10] but we wish to emphasize its importance as a diuretic to initiate the flow of urine.

The object of the experiments reported here was to test the efficacy of hypertonic solutions of dextrose in stimulating diuresis. Different strengths of dextrose solutions ranging from 4 to 23 per cent were used in an effort to find an optimum concentration for the purpose in mind. The dextrose content of the blood and that of the urine were determined after the injection to see if there was any relation between diuresis and hyperglycemia or between diuresis and glycosuria. The principal acid and base constituents of the blood were determined before and after treatment to supplement a clinical evaluation of the efficacy of the therapy.

MATERIAL

Fifteen infants were studied in this series. They all presented a picture of severe gastro-intestinal intoxication with diarrhea, dehydration and acidosis. In all but three instances, the carbon dioxide content of the serum was below 40 per cent by volume before the institution of treatment. The infants were placed on a special metabolism mattress [11] immediately after admission to the hospital in order to permit the accurate collection and measurement of urine. Whenever the clinical condition permitted, the infants were observed for from six to twelve hours prior to the institution of treatment in order to estimate the degree of oliguria. In certain extremely sick infants, this was impossible, and it was necessary to rely on the history of anuria obtained from the mother. All of the infants showed some degree of oliguria, and several had had anuria of varying duration.

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10. Dunn, C. H.: Intravenous Glucose Injections in Infancy, Am. J. Dis. Child. **14**:32 (July) 1917. Marriott, W. McK.: Some Phases of the Pathology of Nutrition in Infancy, ibid. **20**:461 (Dec.) 1920. Powers, G. F.: A Comprehensive Plan of Treatment for the So-Called Intestinal Intoxication of Infants, ibid. **32**:232 (Aug.) 1926.

11. Hoag, L. A.: Apparatus for the Quantitative Collection of Urine and Stools in Male Infants, Am. J. Dis. Child. **44**:770 (Oct.) 1932.

Treatment consisted of a hypodermoclysis of 0.9 per cent sodium chloride solution (20 cc. per pound [453.6 Gm.] of body weight), followed by an intravenous injection of dextrose solution (10 cc. per pound of body weight). This was repeated in from seven to twenty-four hours, with further repetitions as indicated by the clinical condition. In four control cases, no dextrose was given. Saline solution was given both subcutaneously and intravenously to two infants; the other two received saline solution only subcutaneously. Blood transfusions were not given until the third day. The treatment was standardized as far as possible to permit a comparison between individual patients of the series. The dextrose content of the solution was determined accurately, and the solution was administered at a constant rate, with a three-way stopcock attached to a Luer syringe. The rate of injection was always greater than the tolerance rate, varying from 2 to 14.6 Gm. per kilogram per hour.

Food was withheld for from eighteen to twenty-four hours and then consisted of curd protein milk (1½ ounces [46.6 Gm.] per pound of body weight in twenty-four hours). The water intake by mouth varied. In four cases of the dextrose series and the four control cases, it was withheld for twenty-four hours in order that the efficacy of the dextrose solution in promoting diuresis might be more clearly demonstrated.

METHODS

The methods for the determination of the acid-base status of the serum were the same as those used previously.[4e] The Shaffer-Hartmann[12] method was employed for the determination of sugar, and analyses were made on capillary blood taken from the heel. The Folin[13] method was used for the determination of sugar in the urine and in the solutions used for injection. Each specimen of urine was analyzed separately. During the day, the samples were analyzed at once. The night specimens were preserved with toluene and placed on ice immediately for analysis the next morning.

RESULTS

Table 1 presents the results of the chemical analysis of the blood before and after treatment. These data were used to supplement clinical observations in appraising the value of the therapy. In the first eight cases, the treatment was by hypodermoclyses of 0.9 per cent sodium chloride and intravenous injections of dextrose solutions. In all these cases clinical improvement followed and in six there was a definite increase in the carbon dioxide content of the blood. Case 6, in which there was no immediate improvement, was complicated by hemorrhagic nephritis, which delayed eventual recovery. Except in this one case, all abnormally high nonprotein nitrogen values showed a distinct and rapid drop to normal, suggestive of a reestablishment of normal renal

12. Shaffer, P. A., and Hartmann, A. F.: The Iodometric Determination of Copper and Its Use in Sugar Analysis: II. Methods for the Determination of Reducing Sugars in Blood, Urine, Milk, and Other Solutions, J. Biol. Chem. **45**: 365, 1921.

13. Folin, O., and Berglund, H.: A Colorimetric Method for Determination of Sugars in Normal Human Urine, J. Biol. Chem. **51**:209, 1922. Folin, O.: The Determination of Sugar in Blood and Normal Urine, ibid. **67**:357, 1926.

TABLE 1.—*Chemical Analysis of the Serum in Cases of Dehydration Before and After Treatment*

Case	Date	Time	Serum p_H	Serum $BHCO_3$, M.Eq.*	Serum Chloride, M.Eq.	Serum Protein, M.Eq.	Total Acid Determined, M.Eq.	Serum Total Base, M.Eq.	Undetermined Acid, M.Eq.	Serum Nonprotein Nitrogen, Mg. per 100 Cc.	Treatment†
1	1/20/30	10 p.m.	....	10.3	102.3	23.9	136.5	116.5	....	73.1	Before treatment
	1/23/30	10 a.m.	7.52	15.0	110.4	14.3	139.7	138.4	....	36.0	Saline, 840 cc.; dextrose, 350 cc.
2	5/22/29	3 p.m.	7.43	14.8	104.0	13.4	132.2	138.9	6.7	24.0	Before treatment
	5/26/29	4 p.m.	7.40	23.3	102.2	10.5	136.0	145.8	9.8	....	Saline, 640 cc.; dextrose, 273 cc.
	6/ 6/29	10 a.m.	7.35	20.5	96.0	14.1	130.6	140.1	9.5	....	After recovery
3	5/16/29	10 a.m.	7.37	13.8	105.5	15.2	134.5	.....	....	26.3	Saline, 125 cc.; dextrose, 72.5 cc.
	5/18/29	3 p.m.	7.45	18.2	106.9	16.1	141.2	159.0	17.8	....	Saline, 600 cc.; dextrose, 187.5 cc.
	6/ 6/29	3 p.m.	7.51	24.4	.....	17.7	.....	152.8	....	....	After recovery
	6/10/29		7.47	23.4	.....	17.5	.....	.....	....	....	After recovery
4	11/13/29	11 a.m.	7.33	14.4	93.4	15.3	123.1	134.2	11.1	74.2	Before treatment
	11/14/29	3 p.m.	7.44	15.2	103.7	13.3	133.2	149.2	17.0	28.1	Saline, 480 cc.; dextrose, 240 cc.
5	6/13/29	10 a.m.	7.36	20.6	93.6	18.8	133.0	143.6	10.6	64.7	Before treatment
	6/17/29	10 a.m.	7.32	14.2	103.7	13.4	131.3	142.5	11.2	16.9	Saline, 750 cc.; dextrose, 375 cc.
6‡	9/12/29	11 a.m.	7.34	18.8	76.1	23.6	118.5	143.4	24.9	117.0	Before treatment
	9/14/29	11 a.m.	7.28	14.4	93.2	15.1	122.7	143.2	20.5	....	Saline, 825 cc.; dextrose, 450 cc.
	9/15/29		....	14.0	98.7	....	.....	.....	....	132.2	
	9/17/29		....	12.4	110.5	....	.....	.....	....	55.6	
	9/21/29		7.33	10.9	117.2	15.3	143.4	.....	....	....	
	9/30/29		7.48	21.0	105.5	18.7	145.2	.....	....	27.8	After recovery
7	7/11/29	4 p.m.	7.23	8.0	101.8	18.1	127.9	127.9	....	51.2	Before treatment
	7/13/29	8 p.m.	7.35	12.7	107.8	13.3	133.8	136.2	2.4	21.7	Saline, 600 cc.; dextrose, 167 cc.
	8/ 1/29		7.45	21.3	107.9	14.0	143.2	153.5	10.3	....	After recovery
10	12/ 6/29	12 noon	7.32	9.8	103.8	17.2	130.8	145.0	14.2	151.6	Before treatment
	12/ 7/29	2 p.m.	7.41	13.1	114.0	10.9	138.0	148.0	10.0	79.1	Saline, 650 cc.; dextrose, 340 cc.
	12/23/29		7.50	18.0	105.4	15.0	138.4	.....	....	26.5	After recovery
12	3/ 7/30	4 p.m.	7.30	16.2	108.5	19.8	144.5	.....	....	74.8	Before treatment
	3/ 9/30	9 a.m.	7.23	19.9	112.9	14.6	147.4	163.3	15.9	20.9	Saline: 198 cc. intravenously; 590 cc. subcutaneously
13	5/13/32	1 p.m.	7.27	14.5	95.5	20.6	130.6	141.6	11.0	....	Before treatment
	5/14/32	1 p.m.	7.22	14.5	123.0	15.9	153.4	164.6	11.2	....	Saline: 160 cc. intravenously; 420 cc. subcutaneously
	5/19/32	9 a.m.	7.45	21.0	110.2	12.6	143.8	147.5	3.7	....	
14	4/ 1/30	2 p.m.	7.33	16.0	95.1	16.2	127.3	133.0	5.7	38.2	Before treatment
	4/ 2/30	4 p.m.	7.22	9.0	146.3	12.5	167.8	175.5	7.7	53.2	Saline, 900 cc.
	4/ 3/30	4 p.m.	7.28	15.3	136.8	11.4	163.5	163.6	0.1	34.8	Dextrose, 300 cc.
	4/10/30		7.48	25.1	101.9	16.7	143.7	.....	....	12.1	After recovery
15	3/26/30	10 p.m.	7.32	11.4	105.7	19.4	136.5	.....	....	....	Before treatment
	3/27/30	4 p.m.	7.12	7.3	123.5	16.1	146.9	.....	....	90.0	Saline, 550 cc.

* $BHCO_3$, base bound by bicarbonate; M.Eq., milliequivalents.

† Saline solution (0.9 per cent sodium chloride) was administered subcutaneously except when otherwise indicated (cases 12 and 13). Dextrose was administered intravenously (table 2 gives the concentrations of the solutions used).

‡ This infant was also suffering from hemorrhagic nephritis.

function. Contrasted with these cases are four in which no dextrose was given for the first thirty hours. In cases 12 and 13 saline solution was administered subcutaneously and intravenously, the total amount of fluid being proportional to that received by infants who were given dextrose. In case 13, there was no change in the carbon dioxide content of the blood, but the chloride content rose to a very high level (719 mg. of sodium chloride per hundred cubic centimeters of serum). In the other case in this group there was an increase in carbon dioxide with a less marked increase in chlorine. In cases 14 and 15 only clyses were given, and the results, as may be seen from table 1, were very poor, the acidosis becoming definitely more marked. Chart 2 shows cases from each group.

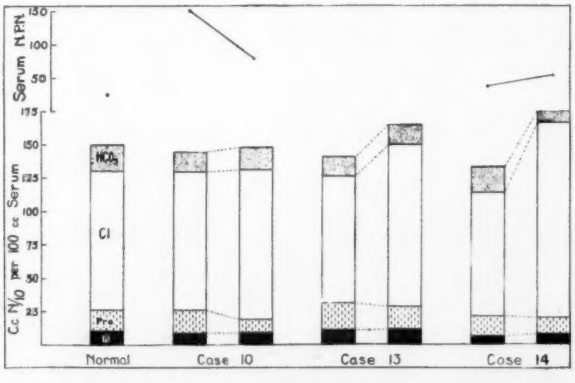

Chart 2.—The acid-base status of the serum before and during the treatment of acidosis in dehydration. In case 10, dextrose solution was given intravenously and saline solution subcutaneously; in case 13, saline solution intravenously and subcutaneously; in case 14, saline solution subcutaneously. In each case, the first column represents the status of the serum before treatment was started; the second column, twenty-four hours later. Only the acid constituents have been plotted, since the sum of these represents the total fixed base of the serum. *R* represents undetermined acid and is the difference between total base and the sum of bicarbonate, chloride and protein.

The purpose of administering hypertonic dextrose solution was to stimulate renal function and to provide water which would become rapidly available for excretion through the kidney. The results are somewhat difficult to evaluate, owing to the very irregular intervals at which the infants voided. An attempt has been made in each case to calculate the amount of urine secreted during the five hours following the completion of the injection. Although this method has many objections, it is a serviceable aid in comparing the diuretic effects of the injections of dextrose. The results are shown in table 2, and typical

TABLE 2.—*Response of Dehydrated Infants to Parenteral Administration of Fluid*

Case	Weight, Kg.	Water by Mouth	Hours After Preceding Injection	Dextrose: Total Gm.	Dextrose: Concentration of Solution, per Cent	Interval of Injection, Min.	Rate of Injection, Gm. per Kg. per Hr.	Urine Volume in 5 Hrs. After Injection, Cc.	Dextrose in 5 Hour Specimen: Per Cent	Dextrose in 5 Hour Specimen: Mg.	Dextrose in 5 Hour Specimen: Per Cent of Intake
1	3.175	No	..	6.454	9.22	24	5.08	11.1	2.08	231.30	3.6
		No	11	6.517	9.31	25	4.98	41.8	1.21	507.88	7.8
		No	4	6.118	8.74	28	4.13	81.3	0.63	513.19	8.6
		No	5	6.454	9.22	23	5.31	109.9	0.43	470.05	7.3
2	3.997	No	..	4.522	5.32	30	2.26	22.8	1.25	285.60	6.3
		No	23.5	8.354	9.18	17	7.38	90.4	0.72	649.08	7.8
		Yes	26	8.070	8.32	40	3.03	191.7	0.34	654.65	8.1
3	3.288	Yes	..	3.756	5.18	16	4.28	15.6	0.13	20.40	0.5
		Yes	17.5	8.625	23.00	13	12.09	52.8	1.15	607.52	7.0
		Yes	20	4.058	5.40	35	2.12	52.1	0.08	42.35	1.0
		Yes	25	3.023	4.03	19	2.90	100.8	0.03	28.93	1.0
4	3.657	Yes	..	8.400	10.50	28	4.92	32.0	0.28	90.05	1.1
		Yes	7	8.240	10.30	10	13.49	48.4	0.51	247.91	3.0
		Yes	16.5	8.240	10.30	12	11.27	193.7	0.26	510.20	6.2
5	5.556	Yes	..	13.000	10.40	12	11.70	40.5	2.27	919.20	7.1
		Yes	7	13.000	10.40	30	4.68	111.7	1.63	1,816.97	14.0
		Yes	16.5	13.000	10.40	34	4.13	87.3	1.86	1,618.62	12.4
6*	6.917	Yes	..	14.160	9.44	30	4.09	45.6	0.68	45.55	0.3
		Yes	20.5	15.075	10.05	15	8.74	48.6	0.42	202.29	1.3
		Yes	8	15.930	10.62	15	9.23	46.2	0.39	176.64	1.1
7	3.458	Yes	..	7.382	13.30	30	4.27	52.4	0.67	351.48	4.8
		Yes	5.5	7.382	13.30	15	8.55	87.0	0.04	37.42	0.5
		Yes	18.5	7.382	13.30	13	9.83	39.0	1.43	556.43	7.5
8	4.331	Yes	..	7.695	8.10	30	3.55	79.0			
		Yes	7	7.838	8.25	15	7.24	130.5			
		Yes	14.5	7.405	7.90	30	3.42	57.8			
		Yes	9	7.125	7.50	15	6.58	71.8			
9	4.082	Yes	..	8.100	9.00	30	3.97	37.3			
		Yes	27	8.550	9.50	28	4.49	42.8			
		Yes	22.5	7.735	9.10	15	7.58	31.7			
		Yes	30	9.605	22.60	14	10.08	31.6			
10	3.799	No	..	17.170	20.20	27	10.04	0			
		No	5.5	15.725	18.50	17	14.62	94.5	2.47	2,336.00	14.9
		Yes	12	18.500	10.00	15	8.95	56.8	0.70	393.50	4.7
11	6.577	No	..	29.290	20.20	30	8.91	33.5	2.40	806.04	2.8
				Effect of Saline Solution (0.9 per Cent Sodium Chloride) Administered Subcutaneously and Intravenously							
12	2.971	No	..	.....	....	..	....	6.3			
		No	18	.....	....	..	....	34.7			
		No	10	.....	....	..	...	48.0			
13	3.486	No	..	.....	....	..	....	7.5			
		No	7	.....	....	..	....	7.5			
				Effect of Saline Solution (0.9 per Cent Sodium Chloride) Administered Subcutaneously (No Other Treatment)							
14	4.629	No	..	.....	....	..	....	0			
		No	7	.....	....	..	....	0			
		No	11.5	.....	....	..	....	0			
15	4.990	No	..	.....	....	..	....	8.5			
		No	13	.....	....	..	....	3.0			

* This infant was also suffering from hemorrhagic nephritis.

cases from each group are graphically illustrated in chart 3. An attempt was made to have the results more comparable in all cases by withholding fluid by mouth. However, the severity of the illness made this unwise in many cases, so, for estimating the diuretic value of dextrose we are justified only in comparing cases 1, 3, 10 and 11, in which dextrose was given, with cases 12, 13, 14 and 15, in which only saline solution was administered. The average volume of urine for the first group was 16.9 cc. per five hours, and for the second group 5.6 cc. per five hours. In all patients receiving dextrose the excretion of urine was greater with each succeeding injection, indicating the replenishment of body fluid reserves so that more water was available for excretion.

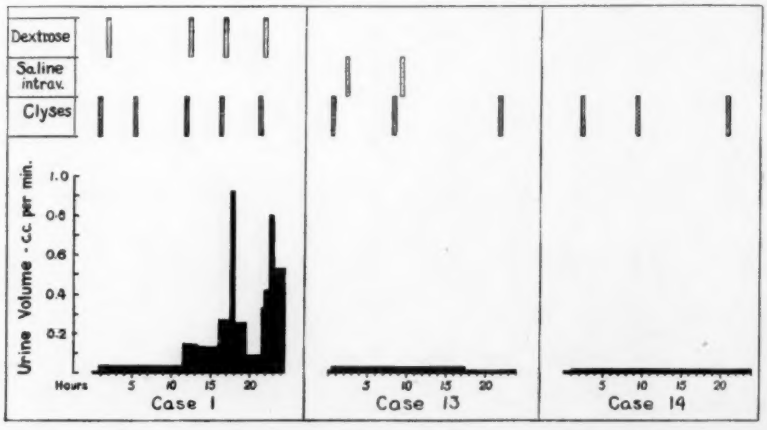

Chart 3.—The urine output of infants suffering from acidosis accompanying diarrhea and dehydration.

An attempt was made to find the optimum strength of solution to promote a beneficial diuresis. For this purpose, solutions varying from 4 to 23 per cent of dextrose were used. From table 2, it may be seen that no such optimum can be predicated from this series of cases. The volume of urine excreted during the five hour period following the injection appears to have no constant relation to the strength of the dextrose solution injected. This is somewhat contrary to expectations, but one might suppose, in these cases, that the output of urine was more dependent on the fluid reserve of the body. There is some evidence as to the validity of this supposition in that the smallest amounts of urine were excreted by infants who had very high protein contents of the serum (cases 1, 6 and 7). In this instance, the protein content of the serum has been used as an approximate indication of the body's fluid reserves, since it yields more serviceable results than the clinical examination of the skin turgor.

From table 2, it is apparent that there is practically no correlation between the rate of injection and the dextrose concentration or content of the urine. There is, as would be expected, some degree of correlation between the dextrose content and the volume of urine.

TABLE 3.—*Blood Sugar Following Intravenous Injection of Dextrose*

Case	Total Dextrose Given, Gm. per Kg.	Rate of Injection, Gm. per Kg. per Hr.	Blood Sugar, Mg. per 100 Cc.					
				After Injection of Dextrose				
			Fasting	½ Hour	1 Hour	1½ Hours	2 Hours	3 Hours
Following First Injection								
1	2.03	5.08	142	374	285	...	197	...
2	1.13	2.26	...	181	95	93	88	91
3	1.14	4.28	...	...	115	...	98	...
4	2.30	4.92	138	246	140	...	79	83
5	2.34	11.70	120	346	278	...	193	141
6	2.05	4.09	138	338	233	...	...	227
7	2.13	4.27	209	350	331	...	214	108
8	1.79	3.58	108	233	119	...	116	104
9	1.98	6.60	124	...	326	...	146	122
10	4.52	10.04	57	406	480	...	510	464
11	4.45	8.91	85	414	530	...	...	...
Average...	2.35	5.98	125	321	267	...	182	168
Following Second Injection								
1	2.05	4.92	...	342	297	...	171	87
2	2.09	7.38	...	238	150	132	100	79
3	2.62	12.09	...	351	233	138	144	139
4	2.25	13.49	...	198	123	...	84	70
5	2.34	4.68	128	341	311	...	246	148
6	2.18	8.74	...	450	309	...	...	131
7	2.13	8.55	108	183	130	...	119	129
8	1.83	7.32	104	228	105	...	91	...
9	2.09	5.23	...	78	67	...	84	105
10	4.14	14.62	...	...	508	...	484	365
Average...	2.37	8.70	...	268	223	...	169	139
Following Third Injection								
1	1.93	4.13	...	284	203	...	136	...
2	2.02	3.03	...	226	...	103	97	94
3	1.23	2.12	...	164	...	89	75	73
4	2.25	11.27	134	306	268	...	132	...
5	2.34	4.13	...	344	315	...	185	129
6	2.30	9.23	141	...	326	...	231	...
8	1.74	4.18	...	213	91	58	96	...
9	2.01	8.04	...	262	154	85	69	67
Average...	1.98	5.77	...	257	226	...	128	91
Following Fourth Injection								
3	0.92	2.90	...	191	99	73	79	97
8	1.65	6.60	...	133	88	...	80	...
9	2.35	5.88	67	293	234	111	...	85
Average...	1.64	5.13	...	206	140	92	80	91

The sugar content of the blood was observed in eleven infants after thirty-two injections. The results are given in table 3. In general, it may be seen that the level of the blood sugar during fasting was somewhat above normal and the return to the fasting level delayed in these as compared with normal infants. This is in agreement with the report

of studies made by Tisdall, Drake and Brown [14] on infants suffering from acute gastro-intestinal intoxication. There seemed to be no relation between the hyperglycemia and the diuresis.

COMMENT

The etiology of diarrhea in infants is obscure, and it is not our purpose to discuss it. We are concerned with the effects of the diarrhea on the infant and the most advantageous method of overcoming such effects. The principal symptoms in severe gastro-intestinal intoxication which require immediate treatment are dehydration and acidosis. The etiology of these two syndromes is fairly well understood. Certainly, the dehydration results from abnormal loss of water from the body owing to diarrhea and vomiting and is frequently accentuated by an inadequate intake of fluid. Diarrhea also causes a drain of inorganic salts from the body, principally basic ions since their route of excretion is, normally, through the stools. Were acid ions excreted in the urine in a normal proportion, the body would suffer merely from deprivation of water and salt, the total fluid remaining in the body having a normal salt concentration. However, in severe dehydration, the volume of urine is scanty, so that the acid ions are not adequately excreted. This retention of acid ions is, undoubtedly, one of the principal causative factors in the development of acidosis.

Treatment must, therefore, fulfil the following requirements: (1) provide an adequate supply of water, (2) stimulate renal function in order that excess acid ions may be excreted and (3) replenish the salt stores in the body.

The treatment which has been used at the New York Nursery and Child's Hospital for the last sixteen years consists of subcutaneous injections of physiologic solution of sodium chloride (0.9 per cent) and intravenous injections of hypertonic dextrose solution (usually 10 per cent). The dextrose solution is used primarily as a mild diuretic to stimulate the flow of urine. That it performs this function may be seen from the data presented in this paper. The average output of urine for five hours after the first treatment in cases 1, 2, 10 and 11, in which dextrose and saline solutions were given, was 16.9 cc. as compared with an average of 6.9 cc. in cases 12 and 13, in which proportional amounts of fluid were given but all in the form of sodium chloride solution (table 2).

Comparison of the immediate effect of these two forms of treatment on the acid-base status of the blood is difficult, since the second

14. Tisdall, F. F.; Drake, T. G. H., and Brown, A.: The Carbohydrate Metabolism of Infants with Diarrhea, Infections and Acute Intestinal Intoxication, Am. J. Dis. Child. **30**:837 (Dec.) 1925.

analysis of the blood was usually made several days after the first and after administration of food and water by mouth had been started. In the two patients receiving saline solution intravenously and subcutaneously (cases 12 and 13), the second analysis of the blood was made before any other type of treatment had been instituted. In both of these, there was a distinct increase in the chloride content of the serum. The acidosis became definitely more severe in case 13, owing to the marked retention of chloride (719 mg. of sodium chloride in 100 cc. of serum).

It seems, therefore, that the combination of hypodermoclyses of isotonic saline solution and intravenous injections of hypertonic dextrose forms a therapy which will usually fulfil the requirements for early treatment, namely, provide the body with fluid and electrolytes and stimulate diuresis so that excess acid may be more readily excreted. Even in the presence of continuing diarrhea, this treatment did not lead to an abnormal accumulation of chloride or a lowering of the bicarbonate content of the serum. Previous work [4c] has shown that the same treatment did not increase the relative loss of fixed base from the body, since the increased secretion of urine was adequate to maintain a normal ratio of electrolytes lost from the body.

It must be emphasized that the use of hypertonic dextrose solutions is advisable only during the earlier stages of dehydration when oliguria or anuria is present. Once an adequate flow of urine is established and can be maintained by administration of fluids the use of a diuretic solution would only defeat the purpose of further attempts to replenish body water.

CONCLUSIONS

The oliguria or anuria which is so frequently present in the acute stage of gastro-intestinal intoxication is largely responsible for the accompanying acidosis, since it leads to a retention of acid ions in the body. The primary aim of the initial treatment should therefore be the restoration of an adequate flow of urine. Hypertonic solutions of dextrose administered intravenously serve this purpose. When combined with hypodermoclyses of saline solution they fulfil the three desiderata of immediate treatment by furnishing fluid and electrolytes and stimulating renal function. Improvement in clinical condition and acid-base status of the blood has resulted from this treatment.

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INDICATIONS THAT MONGOLOID IMBECILITY IS A GAMETIC MUTATION OF DEGRESSIVE TYPE

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ST. LOUIS

Whether a mutation, even a degressive mutation, the result of a disturbance in the biologic order at the beginning of life, with its inevitable limitation of function as well as change in anatomy, may constitute disease may be open to question. The term is used in this paper chiefly because of its convenience, although I believe that any pathologic syndrome such as mongolism is in fact a "departure from health," which is the definition of disease commonly found in modern dictionaries.[1]

THREE SIGNS OF MONGOLISM

Figure 1 shows the astonishing elasticity of the skin in mongolism. The added peculiarity of redundancy makes it a useful sign of this disease. This combination is often best appreciated in the neck, especially the back of the neck, where the folds with their familiar feel may be grasped and lifted away from the underlying muscles.

The soft skin of the mongoloid imbecile, its fulness, one might say its amplitude, is of great diagnostic value. In the female, the labia majora exhibit this peculiarity so often as to afford another sign of this disease. When these characteristics are pronounced, the labia resemble small round pillows and may be quite distinctive.

A third sign of mongolism comprises the peculiarities of the nipples. They are tiny, round beads placed on a flat surface. There is a relative absence of areola. Only occasionally is this condition of help in diagnosis, although when present it may render assistance. None of these items is pathognomonic of mongolism; they may be seen in

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Read before the St. Louis Pediatric Society, Dec. 16, 1932.

From the Washington University School of Medicine and St. Louis Children's Hospital.

1. Dorland, W. A. Newman: The American Illustrated Medical Dictionary, ed. 12, Philadelphia, W. B. Saunders Company, 1923. Webster: The Peerless Dictionary, Springfield, Mass., G. & C. Merriam Company, 1930.

varying degrees in apparently normal children just as the in-curved little finger which has been deemed a highly important point in the recognition of mongolism was found in about one fifth of the members of a group of persons without mongolism. So far as I am aware, these signs have not been described heretofore.

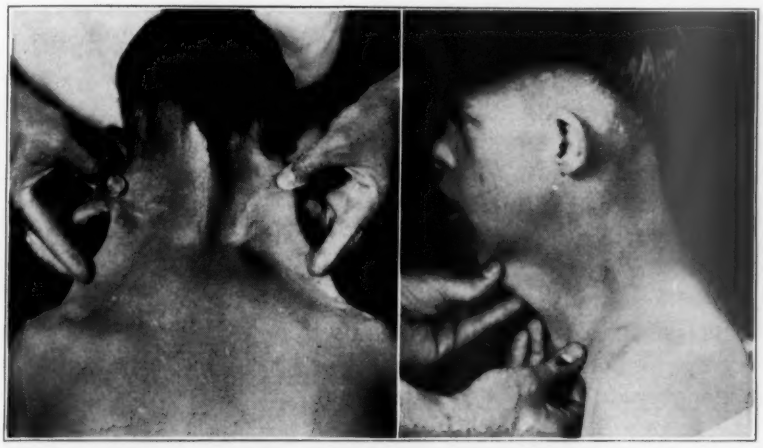

Fig. 1.—Softness, fulness, elasticity and redundancy of the superficial tissues may often be detected in the nucha. When present they afford a convenient and helpful sign of mongolism (Roy H. W. M., aged 10 years).

Fig. 2.—The round, full labia in mongolism. Note also the redundancy of the right thigh. (Baby L., 5 days old, seen with Dr. Park White, Jr., who allowed me to use this picture.)

THE ORIGIN OF MONGOLISM

Looking at mongoloid imbeciles is like looking at the stars; the more one looks, the more one sees. New things are always appearing, and the suggestion is aroused that much more remains hidden from view. Certainly the more one studies these persons, the less one is able to find anything normal about them. It is not unlikely that some time it may

be known that no part of the entire body is spared its own particular distortion by this disease; that no organ or tissue whatever may not reveal evidence of it. It is thus probable that the symptomatology of mongolism is destined to become much more ample than it is now, and that it will be learned that imbecility is only incidental to it, the brain, like any other part of the mongoloid body, exhibiting changes that are always characteristic.[2]

If one may indulge in speculation as to the origin of mongolism, it is likely that one will go back to the embryo to find there perhaps a deviation which was present at the time of fertilization or even before fertilization which would involve the entire structure of the new being. It is thus probable that the problem of mongolism may belong to the cytologist rather than to the common-clay clinician, to whom it may be only a problem in genetics. There are two reasons for this idea: first, the clinical aspects of the disease as mentioned; namely, that the entire body seems to be involved, which, if true, fairly satisfies the requirements of a gametic origin, and second, that no two ovum pregnancy has yet been reported in which both children had mongolism, nor any monozygotic pregnancy the result of a double sperm implantation of one ovum with a single chorion and children of the same sex in which one child was a mongoloid imbecile and the other was not. Alone these facts suggest, and combined they fairly indicate, that mongolism occurs with fertilization or has already occurred before it during the period of maturation either of the ovum or of the spermatozoon, and that it is here that elaboration of the subject may be most promising.

RELATED BIOLOGY

It will be recalled that the maturation of both the ovum and the spermatozoon preparatory to fertilization is characterized by the appearance of chromatin-bearing bodies known as chromosomes which are identical in number for each species. After the appearance of these bodies and their arrangement along the equator of the cell, half of their chromatin is lost and two new nuclear bodies appear; in each of these a reticulum forms in which the chromatin is again increased. Thus is reached the so-called resting period when paternal and maternal elements, both in the ovum and in the spermatozoon, may be differentiated. On fusion of the two new nuclear bodies, the number of chromosomes is reduced to one-half their original number, constituting the all-important period of reduction whereby mature ovum and mature spermatozoon may each provide half the original number of chromosomes which on fertilization will restore the number characteristic of the species, half of them being derived from each of the parents.

2. Davidoff, L. M.: The Brain in Mongolian Idiocy: Report of Ten Cases, Arch. Neurol. & Psychiat. **20**:1229 (Dec.) 1928.

That these structures and these functions may be visited by some of the vicissitudes to which their progeny the embryo will be exposed, there can be little doubt. One might conceive of a disturbance in the structure or the function of the chromosomes or even perhaps of other parts of the germ cell where functions no less important are now believed to occur [3] which might elaborate itself into disease. Indeed such disturbances in structure and in the functioning of the chromosomes have already been observed—"accidents and irregularities in the nuclear make-up," as the geneticist Herbert Walter called them.[4] He said:

> During the period of unpairing of homologous chromosomes the process may not be clean-cut and complete. A piece of one chromosome may adhere to its mate thus changing its size and composition, or again a fragment of a chromosome during the complicated elimination performance accompanying the marriage ceremony of the germ cells may be shuffled out and lost, thus creating a deficient chromosome. Such accidents to the germ cells would be reflected in all the subsequent mitotic divisions of the cells derived therefrom and a mutation would result. Further, an examination of the nuclear structure of mutants frequently reveals chromosomal irregularities so that an unmistakable relation between the two phenomena undoubtedly exists.

There may be an unequal migration of the chromosomes to the poles of the germ cell during the reduction period which will result in a cell progeny having a number of chromosomes unlike the number present in the parent. An example of this occurs in the evening primrose, Enothera lamarkiana, the chromosomes of which number fourteen, whereas in one of its mutations, Enothera lata, fifteen chromosomes are found, an eight chromosome gamete joining with a normal seven chromosome gamete because, prior to the resting period, the chromosomes divided unequally. In this case instead of fourteen dividing into two groups of seven each, they divided into eight and six, so that when eight were fertilized with a normal germ cell containing seven, it produced the mutant fifteen, a mutation which de Vries called degressive because it was defective and in natural surroundings was incapable of reproducing itself.

A DEFINITION OF MUTATIONS

Perhaps the definition of a degressive mutation may be left to history, extending back to the closing decades of the last century when the terms "variation" and "fluctuation" were used to imply a change in species arising through the force of environment; the whole scheme of inheritance was based on the assumption that peculiarities or modi-

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3. Wilson, Edmund B.: The Physical Basis of Life, New Haven, Conn., Yale University Press, 1923.

4. Walter, Herbert Eugene: Genetics, ed. 3, New York, The Macmillan Company, 1930.

fications acquired through use or disuse might recur in later generations and indeed that transition from one form to another through adaptation to external influences was the most fit of explanations.

Following Darwin's contribution, "The Origin of Species," in 1859, these notions became dominant and remained so for some time despite the fact that new types among both plants and animals were arising abruptly and spontaneously on every hand, which must have been most disconcerting to those who had espoused the creed of natural selection. For these unexpected forms Darwin proposed the term "sport," which continues to be used to this day, although just as he used it, in a more or less tentative, if not apologetic, way. The fact that new types or rather perhaps unknown types could arise spontaneously was the occasion for the mutation theory of de Vries, who found that new species often possessed something not present in the parent; these he called "progressive mutations." There were others which lacked something present in the parent and were therefore called "regressive mutations." Still others were defective and were called "degressive mutations," the degressive mutation being essentially defective throughout its structure and without the normal power of further propagation.

THE MENDELIAN LAW

It is now known that the reappearing types are due merely to genes which for a time had receded from view. Although genes and chromosomes had not been discovered, the term "recessive" had already been coined by Mendel to describe them, a discovery which doubtless far transcends any other contribution to genetics and which at that time, unknown to Darwin, lay slumbering in the archives of an obscure publication in Brunn, Austria.

Since the enunciation of the mendelian laws, it is no longer difficult to account for the reappearance of an unknown type, or even of the progressive or regressive types, the mating of recessive genes from both parents being responsible. The etiology of defective progeny, however, still awaits explanation, and so far as mongolism is concerned, one can at this time do no more than lean on suggestions which clinicians have made in seeking an explanation. These suggestions, it is true, comprise a somewhat formidable and more or less divergent group as is inevitable in so mysterious a situation, and aside from tuberculosis, which was strongly favored as the cause of mongolism by the early English writers, they are fairly represented in the following group:

1. Syphilis: (*a*) in the child and (*b*) the effect on the germ plasm of the parent.
2. Alcoholism in the immediate or remote parentage.
3. Shock during pregnancy or adverse environment of either parent.
4. Social position as a particular example of the latter.

5. Abnormalities of the pituitary sella.
6. Endocrine dysfunction in the child or the parent.
7. Neuropathic inheritance.
8. Consanguinity.
9. Parental age.
10. Race.
11. Sex.

An analysis of these factors by Macklin [5] and by myself [6] has served to arouse the suspicion that satisfactory information relating to the cause of mongolism is not now at hand. Further, it may be noted that the influence of sex, long recognized in relation to mentally defective persons as a class and apparently exhibiting an especially strong influence in mongolism,[7] cannot be accepted as anything more than a contributing factor. Parental age and the old hypothesis of exhaustion so generally quoted by writers on this subject are open to question.[8]

Before leaving this phase of the subject, however, it is especially interesting to recall the belief of Charles Herrman,[9] that mongolism exhibits the behavior of a true recessive unit because of which it may be expected to reappear in the general population from time to time according to the more or less exact ratios of Mendel. Unfortunately, it is in the field of pathology that the celebrated 3:1 ratios are often most difficult to follow, particularly in those diseases in which disruptions in the function of the germ cell may be assumed to have occurred and which may perhaps not duplicate the behavior of a gene of heredity on which mendelian laws are necessarily based. Certainly, however, all available data should be gathered which may bear on so interesting a suggestion.

CONCLUSIONS

1. Three signs of mongolism are described. One of them, redundancy of the folds of the neck, will usually assist in making a diagnosis. The other two are mentioned as of occasional corroborative value.

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5. Macklin, M. T.: Mongolian Idiocy: The Manner of Its Inheritance, Am. J. M. Sc. **178**:315 (Sept.) 1929.

6. Bleyer, Adrien: Concerning the Origin of Mongoloid Imbecility, J. Missouri M. A., to be published.

7. Bleyer, Adrien: The Frequency of Mongoloid Imbecility: The Question of Race and the Apparent Influence of Sex, Am. J. Dis. Child. **44**:503 (Sept.) 1932.

8. Brousseau, Kate: Mongolism, Baltimore, Williams & Wilkins Company, 1928.

9. Herrman, Charles: The Etiology of Mongolian Imbecility, Arch. Pediat. **34**:494, 1917; Mongolian Imbecility as an Anthropologic Problem, ibid. **42**:523, 1925.

Of much greater importance is the desirability of search for additional evidence of this disease, which will be found, I believe, almost anywhere in the body if scrutiny is sufficiently close. Minute anatomy will contribute its part.

2. As to the origin of mongolism, one may perhaps speculate on the existence of an alteration in the normal number of chromosomes, just as this is known to account for the degressive mutations of plants, a very early alteration in the germ cell, a true gametic alteration which would repeat itself in every cell derived therefrom throughout the entire body. The human cell is a forty-eight chromosome cell. Whether in the mongoloid imbecile one is dealing with forty-nine or forty-seven, with fifty or forty-six or with some other number of chromosomes must be left to the cytologist, in whose field the richest prizes in genetics now seem to lie.

Nor is it possible to reject the hypothesis of some other fixed irregularity or disturbance either of anatomy or of function of any part of the germinal cell, of which the chromosomes just now receive the largest share of attention. This irregularity owes its existence to causes not yet understood but capable of producing a defect which in this instance repeats itself with amazing faithfulness. This suggests one cause and one disturbance acting alike in the gamete and all of its progeny. In either case there seems to have been produced a true mutation which, in the language of de Vries, would be called degressive.

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A DRILL FOR LATERAL VENTRICULAR PUNCTURE

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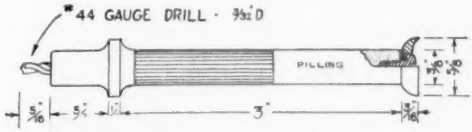
Lateral ventricular puncture is a procedure of recognized value. The method is particularly simple with infants because the unossified coronal suture allows a needle to be inserted directly through it into the ventricle. In older children and adults, however, this route of entry is closed. For such cases, Dandy [1] has devised an operative procedure by which the ventricle may be punctured through a trephine hole made 1 inch (2.5 cm.) above the inion and 1 inch from the midline. This location has been selected by him because the posterior horn of the ventricle is easily accessible from it, and because bleeding is minimal at this point. In childhood, however, ossification of the coronal suture is only partial, so that if some simple means of penetration were available



A drill for lateral ventricular puncture.

it would remain the path of choice for lateral ventricular puncture. I have found a small drill [2] of the type pictured in the illustration a simple aid for this purpose.

The instrument consists of a metal handle in one end of which a three thirty-second inch (no. 44 gage) machinist's drill has been fixed so that the point projects five-eighths of an inch (1.58 cm.). This length has been found sufficient to penetrate safely the skulls of children up to 12 years of age. On the other end a cap is fastened with a machine screw, so that it may rotate freely. The shaft of the instrument is knurled and has an enlargement near the end carrying the drill as a support for the fingers of the operator.

The patient is laid on his back on the treatment table, and the hair shaved over an area about 2 inches (5 cm.) in diameter at the site of the proposed injection. The remaining hair is dampened and brushed

From the Harriet Lane Home of the Johns Hopkins Hospital and the Department of Pediatrics, Johns Hopkins University, Baltimore.

1. Dandy, W.: The Brain, in Lewis, Dean, Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1930, vol. 12, chap. 1, p. 82.

2. The instrument is supplied by George P. Pilling and Son Co., Philadelphia.

tightly to the head away from the site of injection. After the usual sterilization with iodine and alcohol, the skin is infiltrated with procaine hydrochloride about 2 inches from the midline over the ossified coronal suture. An incision one fourth inch (0.61 cm.) in length is made through the skin down to the bone, and the drill is inserted through it. By holding the handle of the drill in the palm of the hand, it is rotated in an intermittent clockwise and counterclockwise motion by the fingertips. Usually the skull is penetrated after a dozen or so rotations. As the tip of the drill is withdrawn from the hole, a 3 inch (7.6 cm.) lumbar puncture needle is inserted simultaneously so as not to lose the location. The needle is then advanced in a line pointing to the inner canthus of the homolateral eye, and the stylet is withdrawn from time to time until the ventricle has been entered.

This procedure has been found satisfactory for children up to 12 years of age. It has been especially helpful for the introduction of serum directly into the ventricles of patients with meningitis. The physiologic flow of spinal fluid away from the choroid plexus aids the diffusion of the serum, so that it is more quickly and easily distributed than when it is injected into the lumbar subarachnoid space. The method should also prove helpful for the injection of air into the ventricles for roentgenographic encephalography.

CONTINUED SPINAL DRAINAGE

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Repeated drainage of the spinal fluid has often been advocated in the treatment of patients having inflammatory conditions of the central nervous system. This therapeutic procedure has a dual basis; first, it aids in the removal from the body of the etiologic organism and its toxic products, and, secondly, it helps to maintain a lowered pressure within the central nervous system. The efficacy of the latter action has been demonstrated by the work of Weed [1] and Kubie.[2]

The simplest method by which such drainage can be accomplished is by lumbar puncture. Lately several workers have advocated continued drainage through a needle left in place for several hours. Retan [3] reported good results when this method was coupled with the intravenous injection of large amounts of hypotonic saline solution, especially in diseases of the central nervous system characterized by perivascular round cell infiltration, such as poliomyelitis and encephalitis. However, there are obvious difficulties encountered when one attempts to keep a lumbar puncture needle in place for several hours, especially in children. For this reason a spinal needle holder has been devised by which any standard lumbar puncture needle can be secured in place in an immovable position.

The needle holder is shown in the illustration. It consists of a thin metal disk, three-fourths inch (1.9 cm.) in diameter, perforated at the center. In a socket over this is a split ball one-fourth inch (0.63 cm.) in diameter that carries on the face of each half a small groove into which a 3 inch (7.6 cm.), no. 18 gage lumbar puncture needle may be inserted. The needle can thus be rotated at any angle and advanced to the desired depth and fastened there by the set screw.

The spinal needle holder is slipped over the shaft of the lumbar puncture needle, the side bearing the set screw first, and advanced com-

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The spinal needle holder is supplied by George P. Pilling and Son Co., Philadelphia.

From the Harriet Lane Home of the Johns Hopkins Hospital and the Department of Pediatrics, Johns Hopkins University, Baltimore.

1. Weed, L. H.: Am. J. Anat. **32**:253 (Sept.) 1923.
2. Kubie, L. S.: Brain **51**:244 (June) 1928.
3. Retan, G. M.: New York State J. Med. **31**:1378 (Nov. 15) 1931; Forced Spinal Drainage in Relation to Infections of the Central Nervous System, J. A. M. A. **99**:826 (Sept. 3) 1932.

pletely to the hilt, where it is temporarily fastened. The lumbar puncture is then done in the usual way. When the spinal fluid is flowing freely, the stylet is reinserted, the set screw released and the needle holder slid down the needle until it rests against the patient's back. The ball and socket allow the holder to assume any required angle to the needle, and the set screw tightens it firmly in place. Four strips of adhesive (3 by ½ inch [7.6 by 1.27 cm.]) are then used to fasten the holder securely to the body.

I first allowed the spinal fluid to escape unhampered, or controlled its flow by reinsertion of the stylet at intervals. However, vomiting and headache are liable to ensue if the spinal fluid pressure is too greatly or too rapidly depressed. For this reason an escape manometer has been connected to the needle. This is simply an inverted J tube of glass attached to 2 feet (60.96 cm.) of light rubber tubing. The other end of the tubing is joined to the lumbar puncture needle by means of a two-

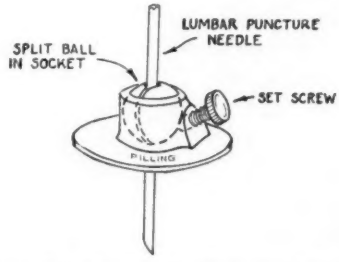

Diagram of holder for lumbar puncture needle.

way stop-cock with a Luer adapter. Immediately after the lumbar puncture, the manometer is elevated until the flow is not more than 1 drop per second. This rate gradually decreases as the spinal fluid escapes, and the manometer is lowered from time to time, depending on the rate of flow, until its tip is from 5 to 10 cm. above the needle. This maintains about half the normal spinal fluid pressure.

A certain difficulty is encountered in keeping the child in proper position. Older children are placed on a Bradford frame or restrained on the side by securing the elbows and knees with soft gauze bandage. This allows enough freedom of the hands and feet for comfort, although the patient cannot turn on his back. The same method is also satisfactory for small children, but infants can be more easily controlled in a hammock. This is made of light canvas with a 3 inch hole in its center, and is suspended between the ends of a crib. After the lumbar puncture, the child is placed in the hammock so that the neeble projects through the hole. With reasonable watching, either of these methods of restraint is quite satisfactory.

This method of continued spinal drainage has been employed on a number of children with tuberculous meningitis in order to relieve the symptoms resulting from increased intracranial pressure. The needle was left in position for twenty-four hour periods, then removed and resterilized. After an hour or two, the drainage was again instituted. If the flow of spinal fluid became obstructed before the twenty-four hour period was completed, the course was interrupted and the drainage begun over again. This rarely happened, however, and on several occasions the needle was allowed to remain in place uninterruptedly as long as three days. It was not uncommon to recover over 500 cc. of spinal fluid in a twenty-four hour period, although the output per day gradually decreased. The longest total time of drainage has been five days.

This method offers a simple procedure for the continued drainage of the subarachnoid space in inflammatory conditions of the central nervous system.

TRANSVERSE BANDS IN THE BONES OF A TUBERCULOUS CHILD

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AND
I. RUBELL, M.D.
CHICAGO

Transverse lines in the long bones of children, sometimes called the lines of von Looser, are not infrequently demonstrated in roentgen films. These lines are seen not only in children but also in infants and even in the new-born. A number of observers [1] have attempted to correlate the markings with a deficiency disease, such as rickets. Their opinion receives support from experimental rickets, in the healing stages of which lines such as those mentioned appear. However, lines of von Looser may occur in conditions other than specific vitamin deficiencies. For instance, severe infections, anemias, malnutrition and the administration of phosphorus may give rise to the roentgen appearance observed by von Looser and others in rickets.

An illustrative case, due presumably to the effects of a tuberculous infection or to administration of phosphorus has been encountered by us, which because of the generalized involvement appears to warrant reporting.

REPORT OF CASE

A well developed white boy, aged 9 years, has been under a pediatrician's care from birth. He received the usual antirachitic and antiscorbutic prophylaxis. The early developmental history was normal, and the environment was of the best. In view of these facts, it is hard to assume that there ever existed in this child rickets sufficiently severe to account for the bands and for the absence of ossification of several centers at the age of 9 years. This leads us to feel that rickets and scurvy may be excluded as possible etiologic factors, although many workers, especially Hess, have shown that a condition such as late rickets may be present.

The patient came under our observation because of mild pain in the right hip joint; examination revealed only slight muscle spasm and slight limitation of abduction. There was, however, a rise in the temperature in the afternoon and the child was hospitalized for observation. Roentgenograms were ordered. The Pirquet and Mantoux tests were strongly positive. Our impression was that a

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From the Orthopedic and Pediatric Service of the Mount Sinai Hospital.

1. Hess, A. F.: Rickets, Including Osteomalacia and Tetany, Philadelphia, Lea & Febiger, 1929. Pappenheimer, A. M.: Experimental Rickets in Rats, J. Exper. Med. **36**:335, 1922. von Looser, E.: Ueber Spaetrachitis und Osteomalacia: Klinische, röentgenologische und pathologisch-anatomische Untersuchungen, Deutsche Ztschr. f. Chir. **152**:210, 1920.

Fig. 1.—Transverse bands in the vertebrae, pelvis and upper ends of the femur.

Fig. 2.—Curved lines in the epiphyses and transverse bands in the lower end of the femur and upper ends of the tibiae and fibulae.

Fig. 3.—Transverse bands in the radii, ulnae (seen in right ulna) and metacarpal bones; also curved lines in the centers of ossification and presence of only three centers in the wrist.

Fig. 4.—Transverse bands in the tibiae, fibulae and metatarsal bones; also curved lines in the os calcis, astragalus and cuboid.

tuberculous process of the hip joint was present, and this diagnosis was confirmed by inoculation of the fluid obtained from the hip joint into guinea-pigs. Previous to this there had been no definite roentgen evidence of the infection. The factor that led us to a further investigation was the peculiar double transverse bands in the femur and the ilium. Chemical analysis of the blood for calcium and phosphorus revealed that both were within normal limits, the former being 10.8 mg., and the latter 3.2 mg., per hundred cubic centimeters of blood. Other facts of interest were that roentgenologically and clinically the lungs showed no evidence of an active tuberculous process, although there was marked hilar infiltration. At no time has the child appeared very ill; he has never been in a state of malnutrition, and repeated examinations of the blood have revealed no signs of anemia.

The transverse bands are symmetrically placed in the bones; that is, if they are found in a bone on one side, they are found in a similar situation in the corresponding bone of the opposite side. Examination of the roentgenograms of the entire body revealed that the bands are more conspicuous in the bones where the growth is the greatest. The bands appear more marked in the lower end of the femur, the upper end of the tibia and the fibula, the lower end of the radius and the ulna, the pelvis and the nuclei of the epiphysis.

In the pelvis, vertebrae and the epiphyses, the bands corresponding to the transverse bands in the shaft lie just inside the outer margins of the centers of ossification and are curved exactly like the outlines of these centers. In the long bones where the growth is slower, the transverse bands lie close to the cartilage. This is seen when one compares the bands in the lower end of the femur and the upper end of the tibia or in the upper and the lower ends of the femur. The transverse bands are parallel to the ends of the bones. The distance between them varies according to the growth of that portion of the bone, and the width of the bands appears to vary with the size of the bone. This is exhibited when one compares the roentgenograms of the lower end of the ulna and the radius and the upper end of the tibia and the fibula.

On studying the roentgenograms of the wrist and the foot of this child one notices immediately that there are only three centers of ossification in the wrist. In a child of this age (9 years), all the centers except the pisiform bone should have been ossified. Cohn, Kreuscher and Poland [2] showed that the os capitatum, os triquetrum and the cuneiform bones ossify at this age and can be visualized in the roentgenogram. We also perceived that with the development and growth of these bones curved bands became visible at the outer margins of the nuclei of ossification corresponding to the transverse bands in the long bones. The fact that only three centers are present indicates that some injury to the skeletal development occurred between the ages of 2 and 3. Likewise the bones of the foot that ossify before the age of 3 exhibit the same marking as described in the carpal bones of the hand, and those which appear after this age do not show any of the curved lines at the outer margins of the centers.

It would be appropriate at this point to describe briefly the normal growth of bone. Growth of bone takes place from the ossification of the cartilage cells in the epiphysis. The change from cartilage to bone is at the zone of calcification, while the cells in the zone of

2. (*a*) Cohn, I.: Normal Bones and Joints, New York, Paul B. Hoeber, Inc., 1924. (*b*) Kreuscher, P. H.: A Study of the Development of the Epiphysis, Surg., Gynec. & Obst. **27**:480, 1918. (*c*) Poland, J., quoted by Cohn.[2a]

proliferation are continually multiplying during the period of longitudinal growth. The transverse lines seen in the roentgenograms are caused by modifications of growth. These are ably described by Eliot, Souther and Park,[3] who state that they are not certain as to various details in the development of the transversely disposed trabeculae which are the basis of the lattice formation in the bones, but that they believe that the general principles are clear. The formation has its origin at the junction of the cartilage and the shaft. The growth of the cartilage is suddenly slowed or stopped, and as a result the bone-building energy of the shaft concentrates at a single level or at very slowly changing levels and discharges itself in a more lateral direction than usual. The result is the formation of trabeculae which extend transversely or are actually joined to neighboring trabeculae by cross branches. When the growth of the cartilage becomes reawakened, the trabeculae with the ordinary parallel longitudinal arrangement are again formed, and the lattice is left behind in the shaft. Under ordinary conditions, when the rate of growth is constant, the depth of the proliferating zone remains constant. When the growth of the cartilage slows or stops, the blood vessels and the marrow cells continue to advance through the ripe portion of the cartilage and to convert the latter into a shaft. The end of the shaft thus moves to a position closer to the generating portion of the cartilage, and the depth of the proliferating zone is greatly shortened.

COMMENT

According to the literature, disturbances in the growth of the bones such as those described in this case may be caused by deficiency diseases, such as rickets, scurvy or any chronic debilitating condition. From a study of the case it would be fair to assume that the hindrance to the growth of the bones took place between the ages of 2 and 3, because only three centers of ossification are seen in the wrist and foot which exhibit the curved bands corresponding to the transverse bands in the long bones, and because the centers which ossified at a later date do not reveal these transverse bands.

From the history and physical examination in this case there is no evidence that the patient ever suffered from rickets or scurvy. The history was carefully investigated as to phosphorus having been given, and none, so far as known, was ever administered to the child. Phosphorized cod liver oil, which was in vogue at that time, may have

3. Eliot, Souther and Park: Transverse Lines as Seen in X-Rays in Long Bones of Children, Bull. Johns Hopkins Hosp. **41**:364, 1927.

been given. Phemister [4] quoted Wegner, who showed that the dense layer forming in the ends of the shaft varies in thickness with the length of the period of the administration of phosphorus. If this is so, why do we not see these bands more often?

As the patient now suffers from a proved active tuberculosis of the hip joint, one is tempted to assume that the tuberculous infection may have been present in a latent form since early childhood, and that it constituted the etiologic factor in this instance. One hesitates to consider this case as offering definite proof of a correlation of tuberculosis with the formation of these transverse bands. We feel, however, that in this case, in which no evidence exists other than the known tuberculosis of the hip joint, there may be a definite relationship between the two.

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4. Phemister, D. B.: The Effect of Phosphorus on Growing, Normal and Diseased Bones, J. A. M. A. **70**:1737 (June 8) 1918.

Case Reports

APLASTIC ANEMIA

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Aplastic anemia was first described by Ehrlich [1] in 1888. Since then a change in the nomenclature has been suggested by Frank,[2] who terms the disease hemorrhagic aleukia and panmyelophthisis. Pappenheim [3] also considers the term aregenerative anemia more descriptive of this condition. A study of this case is presented because of the unusually small number of cases reported in the literature and because of the many uncertainties which still surround this condition. It is hoped that light may be shed on this disease by a study of the clinical and hematologic pictures and of the pathologic changes presented in the case reported. The cases of idiopathic aplastic anemia reported in the literature up to the present may be divided into three groups, depending on the presence or absence of pathologic studies and on the final outcome of the case. The first group comprises those cases in which there are all the clinical and hematologic signs of aplastic anemia and in which recovery occurs. In this group belong the cases of Benecke,[4] Parkinson [5] and Hermann.[6]

The second group consists of cases with all the clinical and hematologic evidence of aplastic anemia, without recovery, in which necropsies or studies of the bone marrow were not made. In this group belong the cases of Bruce,[7] Acuña,[8] Babonneix and Tixier,[9] Khàrina,[10] Kleinschmidt [11] (two cases), Larrabee,[12] Rennie,[13] Türck,[14] Parkinson [15] and Franklin.[16]

From the Pediatric Service of the Israel Zion Hospital.

1. Ehrlich: Charité-Ann. **13**:300, 1888.
2. Frank, E.: Berl. klin. Wchnschr. **52**:961, 1915.
3. Pappenheim, quoted by Baar and Stransky.[17]
4. Benecke: Therap. d. Gegenw. **19**:14, 1917, quoted by Hermann.[6]
5. Parkinson: Proc. Roy. Soc. Med. **11**:15, 1917.
6. Hermann, C.: Idiopathic Aplastic Anemia, Am. J. Dis. Child. **23**:484 (June) 1922.
7. Bruce: Arch. Pediat. **44**:659, 1927.
8. Acuña, quoted by Hermann.[6]
9. Babonneix and Tixier: Bull. et mém. Soc. méd. d. hôp. de Paris **35**:227, 1913.
10. Khàrina-Marinucci: Pediatria **23**:101, 1915.
11. Kleinschmidt, H.: Jahrb. f. Kinderh. **90**:161, 1930.
12. Larrabee, R. C.: Am. J. M. Sc. **142**:57, 1911.
13. Rennie: M. J. Australia **1**:485, 1919.
14. Türck, quoted by Hermann.[6]
15. Parkinson: Proc. Roy. Soc. Med. **12**:72, 1918.
16. Franklin: J. M. Soc. New Jersey **27**:262, 1930.

The third group is comprised of cases in which all the clinical and hematologic evidence of aplastic anemia is present; recovery does not occur, and the clinical diagnosis is confirmed by autopsy and studies of the bone marrow. According to the views of Baar and Stransky [17] and Hirschfield,[18] only the cases which make up the last group may be strictly considered as true cases of aplastic anemia. Thus far only fifteen such cases, including the one herein presented, have been reported in the literature, by Babonneix and Paisseau,[19] Babonneix and Tixier,[9] Görter,[20] Heubner,[21] Kleinschmidt [11] (two cases), Smith,[22] Thursfield,[23] Muir,[24] Agnew,[25] Benecke,[26] Mead,[27] Orrico,[28] Young [29] and myself.

The cases of hemorrhagic aleukia or aplastic anemia reported in the literature as being due to benzol, arsphenamine, bismuth or roentgen therapy are not included, since this report concerns itself only with so-called cryptogenic or idiopathic aplastic anemia.

REPORT OF A CASE

History.—S. B., a girl of Jewish extraction, was born at full term and normally delivered. She weighed 7 pounds and 11 ounces (3,487 Gm.) at birth and was breast fed for ten months. She was well until 16 months of age, when she had an attack of tonsillitis with swelling of the cervical glands. On Feb. 9, 1931, immediately following the attack of tonsillitis, the mother noticed that the child looked pale and, on the advice of her family physician, she sent the child to a hospital, where it was found that the hemoglobin content of the blood was 31 per cent. A transfusion was given, and the child was discharged several days later improved; at this time, the hemoglobin content had risen to 58 per cent. The child was apparently in good health until May 15, when an injection of toxin-antitoxin was given; this was almost immediately followed by an elevation of temperature to 102 F., and the arm at the site of the injection became red and swollen. The temperature remained elevated, and the child became restless and did not sleep well. The mother noticed a change in the color of the patient, and said that the skin was muddy brown. The child was then readmitted to the hospital for treatment, and another transfusion was given. The general condition, however, became worse

17. Baar and Stransky: Die klinische Haematologie des Kindesalters, Vienna, Franz Deuticke, 1928.

18. Hirschfeld, quoted by Baar and Stransky.[17]

19. Babonneix and Paisseau, quoted by Hermann.[6]

20. Görter, quoted by Hermann.[6]

21. Heubner, O.: Folia haemat. **19**:347, 1915.

22. Smith, L. W.: Report of an Unusual Case of Aplastic Anemia, Am. J. Dis. Child. **17**:174 (March) 1919.

23. Thursfield: Brit. M. J. **2**:873, 1921.

24. Muir: Brit. M. J. **2**:909, 1900.

25. Agnew: Canad. M. A. J. **14**:859, 1924.

26. Benecke: Folia haemat. **21**:263, 1917.

27. Mead: J. South Carolina M. A. **25**:517, 1929.

28. Orrico: Arch. latino-am. de pediat. **23**:125, 1929.

29. Young: Illinois M. J. **47**:142 (Feb.) 1925.

and, against the advice of her physician, the patient was removed to her home. The diagnosis, on discharge from the hospital, was lymphatic leukemia. At this time, June 5, I was asked to see the child.

Examination.—Physical examination revealed a sick child whose sensorium was perfectly clear, but who was extremely apathetic. There was definite evidence of air hunger; the respirations were rapid and deep. The skin had a dirty brown appearance, but the lips and finger-nails were almost white. The conjunctivae and mucous membranes of the mouth appeared bloodless; the tongue was dry and furred. There was a marked fetor ex oris, and an ulceration of the pillar of the left tonsil, which bled rather freely, was present; there was also a moderate enlargement of the cervical glands on the left side. The axillary, cubital and inguinal glands, however, were not enlarged. The spleen could not be felt, but the liver was palpable two fingerbreadths below the costal margin. Petechiae were present over the flexor surfaces of both forearms; the capillary resistance test was strongly positive. The heart sounds were rapid and regular; a systolic murmur, which was louder at the base and was not transmitted to the axilla, was heard over the entire precordium. The skin was hot, dry and poorly nourished and had the dirty brown pigmentation already described. The temperature was elevated to 104 F.; otherwise the physical examination gave negative results. The child was sent to the United Israel Zion Hospital of Brooklyn, and an immediate transfusion was ordered.

Serologic Observations.—Examination of the blood before transfusion (June 5, 1931) showed the following: red blood cells, 750,000; hemoglobin (Sahli), 10 per cent; white blood cells, 2,200, with polymorphonuclear leukocytes, 8 per cent, lymphocytes, 80 per cent, and lymphoblasts, 12 per cent. The platelets numbered 25,000; there was 1 reticulocyte in 2,000 cells; the bleeding time was ten minutes, and the coagulation time, four minutes. The oxydase reaction was negative.

The patient was given 200 cc. of whole blood intravenously. Temporary improvement followed, as may be seen from the accompanying table and chart 6. Because the child refused fluids or food by mouth, 300 cc. of a 10 per cent solution of dextrose was injected subcutaneously. On June 7, the left cervical gland was definitely smaller, but on June 10 a moderate enlargement of the axillary glands on both sides was noticed. On June 11, the ulcerative process involving the pillar of the left tonsil began to heal. On this day also, 3 ounces (85 Gm.) of an emulsion of fresh bone marrow, in addition to a mixture of milk and egg, was given by gavage. This diet was given daily until June 16, when it was noticed that the ulceration on the tonsil had completely healed, leaving a scar. The child was now able to take food by mouth, and gavage feedings were discontinued. The administration of bone marrow emulsion by mouth was continued until the day of the patient's discharge from the hospital, July 3. At this time, the cervical glands were not enlarged, but a small gland, about the size of a pea, could be felt in the right axilla. The inguinal glands were palpable, but they were no larger than those found in many normal children. The child's general condition and color were good.

During the patient's stay in the hospital, there was an elevation of temperature ranging from 102 to 104 F. from June 5 until June 14, when a drop occurred; from this time until the day of discharge, the temperature ranged between 99 and 100 F. The Wassermann reaction was negative; there was no reaction to 1 mg. of old tuberculin. The urine was consistently normal, except on one occasion, June 9, when the presence of small amounts of urobilinogen, not sufficiently large for quantitative determination, was detected. Cultures of the throat secretions on June 6 and 11 revealed the presence of staphylococci, streptococci and Bacillus

Hematoiogic Observations During First Admission to the Hospital

	June 5	June 6	June 8	June 9	June 11	June 12	June 15	June 18	June 22	July 1
Erythrocytes	750,000	2,000,000	2,450,000	1,750,000	1,750,000	2,900,000	2,900,000	3,100,000	2,900,000	3,450,000
Hemoglobin	10%	40%	45%	40%	34%	50%	54%	55%	60%	72%
Leukocytes	2,200	1,500	2,000	1,900	1,600	1,800	2,100	3,600	5,200	7,400
Polymorphonuclears	8%	12%	12%	10%	13%	42%	40%	34%	65%	58%
Lymphocytes	80%	69%	84%	88%	80%	58%	58%	52%	30%	40%
Lymphoblasts	12%	....	....	....	....	....	....	....	....	....
Eosinophils	....	1	....	....	....	....	....	....	....	....
Basophils	....	2	....	....	....	....	....	....	....	....
Monocytes	....	5%	....	....	1%	....	2%	14%	5%	12%
Türck cells	....	1	....	....	....	....	....	....	....	....
Myelocytes	....	2	....	....	....	....	....	....	....	....
Platelets	25,000	50,000	50,000	35,000	30,000	60,000	60,000	80,000	100,000	150,000
Reticulation	1–1,000	2–1,000	2–1,000	5–1,000	3–1,000	6–1,000	15–1,000	20–1,000	25–1,000	30–1,000
Bleeding time	10 min.	....	....	2½ min.	....	....	....	....	....	....
Clot retraction	9 hrs.	....	....	....	....	....	....	....	....	....
Coagulation	4 min.	....	....	3 min.	....	....	....	....	....	....
Fragility test	....	....	....	....	Began 0.425 Complete 0.350					

proteus. Roentgenologic examination of the long bones on June 9 showed an irregularity on the inner aspects of the lower ends of the femora. There was also some irregularity of the lower ends of both tibias. No rarefaction was present.

In addition to the observations on the blood, as outlined in the accompanying table, it is important to note that on the first examination reticulocytes were almost totally absent, but that there was a slow and definite increase in the number of reticulocytes as time went on. While only 1 reticulocyte in 2,000 red cells was seen on June 5, immediately before transfusion, 1 in 500 was present on the day following transfusion; on June 9, there were 5 in 1,000, and on June 15, 15 in 1,000, and on July 1, 30 in 1,000 red cells were observed. A fragility test, made on June 11, showed that hemolysis began at 0.425 and was complete at 0.35. Some anisocytosis, poikilocytosis and achromia were present in practically all of the blood smears examined. Examination of the blood on July 1, two days before the child was discharged from the hospital, showed 3,540,000 red blood cells, hemoglobin (Sahli) 72 per cent and a white cell count of 7,400, with 58 per cent polymorphonuclear leukocytes, 30 per cent lymphocytes, 12 per cent monocytes, 150,000 platelets and 3 per cent reticulocytes. The mother was advised to continue the administration of fresh bone marrow emulsion at home.

On July 8 the child was brought to me for examination because of a severe cough. There was also a history of poor sleeping and much crying at night. There was a definite enlargement of both submaxillary glands, and fluoroscopic examination revealed an enlargement of the tracheobronchial lymph nodes. The cough was spasmodic and closely resembled the cough of pertussis in the spasmodic stage. The child was again seen on July 15, when she complained of abdominal pain. The submaxillary glands had increased in size, but there was no enlargement of any superficial glands elsewhere, and the spleen could not be felt. The cough was severe and kept the child awake at night. A white cell count showed 30,000 cells, with 44 per cent polymorphonuclears and 56 per cent lymphocytes. On July 22 the cervical glands on the right side became definitely enlarged. The cough was still present, but it was not so severe. Examination of the blood on this date revealed: red cells, 4,200,000; hemoglobin (Sahli), 94 per cent; white cells, 22,000, and platelets, 200,000. The differential count was as follows: lymphocytes, 60 per cent; polymorphonuclears, 35 per cent; monocytes, 2 per cent; myelocytes, 2 per cent, and Türck cells, 1 per cent.

On July 29, the axillary, inguinal, parotid, cervical and submaxillary glands were markedly enlarged. The color of the child had changed; she was pale, and the pigmentation noticed at the first examination had reappeared. The temperature was elevated to 102 F. A purpuric eruption developed over the entire body a few days later, and the child was admitted to the Jewish Hospital, where she remained until September 7.

Second Admission to Hospital.—On September 7, the patient was transferred to the United Israel Zion Hospital. On admission, examination revealed an extremely sick child; the temperature was elevated to 105 F.; the respiratory rate was 45, and the pulse rate, 160. There was bleeding from the mouth, and petechial hemorrhages were present over the entire body; the liver was palpable one-half fingerbreadth below the costal margin, and the spleen one fingerbreadth. There were signs of consolidation of the lower lobe of the left lung. A transfusion of 300 cc. of whole blood was given intravenously. A culture of the blood was made and showed a growth of staphylococci after forty-eight hours.

Examination of the blood on September 7, before the transfusion was given, showed the following: red cells, 1,700,000; hemoglobin (Sahli), 30 per cent; leukocytes, 6,000, with 1 per cent polymorphonuclear leukocytes, 80 per cent lymphocytes

and 10 per cent lymphoblasts; platelets, 20,000, and reticulocytes, 1 to 1,000 red cells. The bleeding time was three minutes and the coagulation time, seven minutes.

An emulsion of bone marrow was again administered. The following day, June 8, the child had a convulsion which lasted fifteen minutes; the twitchings were limited to the left side of the body. This was followed by coma, which persisted until death at 10 p. m. of the same day. The temperature remained constantly elevated during the last stay in the hospital.

Necropsy.—The necropsy report was made by Dr. Max Goldzieher.

The body was that of a poorly developed, emaciated white girl. The skin was considerably mottled, and there were a number of scattered red dots the size of

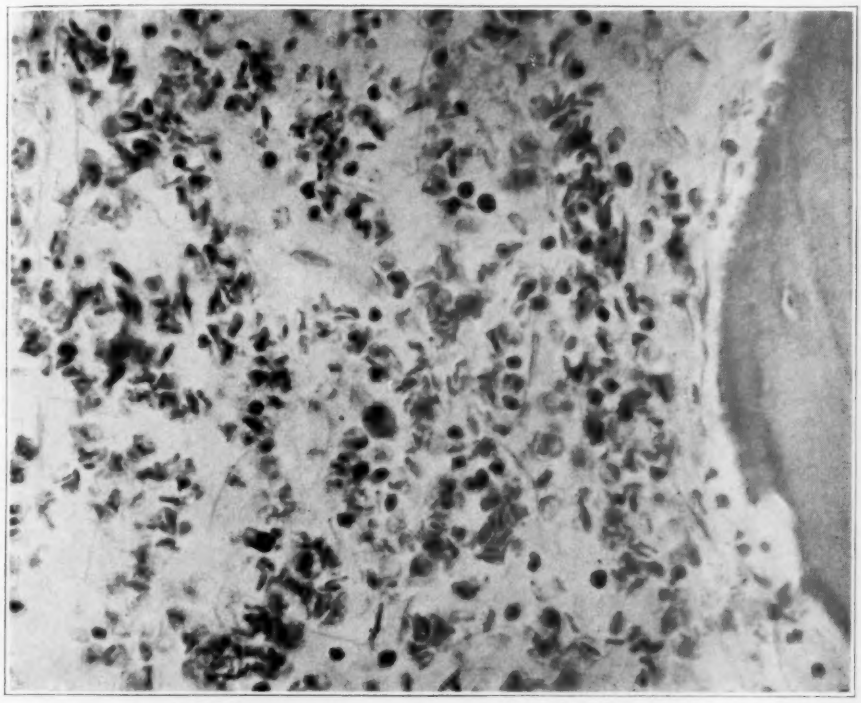

Fig. 1.—Photomicrograph of the bone marrow; low power magnification. The bone marrow is engorged with erythrocytes. There are scanty bone marrow cells and prominent fibrillar reticulum.

a pinhead or larger, particularly over the lower extremities. There were also a number of papular and partly vesicular eruptions, surrounded by a reddish area. The centers occasionally showed a dried yellow crust.

The air content of both lungs was reduced; they were heavy, dark red and nodular to the touch. Some of these nodules bulged out on the surface, and many were yellowish; almost all of the nodules were located beneath the pleura. The surface of the left lung was covered with a fibrinous membrane, which was easily removed. Approximately one-half pint of amber-colored cloudy fluid was present in the left thoracic cavity.

The heart was flabby and collapsed, and the musculature was reddish gray. The valves were thin and smooth. The intima of the aorta was red. The spleen was considerably enlarged; nevertheless, the lower pole of the spleen did not extend below the costal margin. It was red and firm to the touch, and section showed hardly any structure.

The liver extended two fingerbreadths below the costal margin. It was large, firm and a pale pinkish yellow. The structure was well maintained on section; the cut surface was a peculiar yellow-brown.

The bone marrow in the sternum was dark red and when the bone was cut much blood oozed out. The marrow of the tibia was abundant, dark red and quite firm.

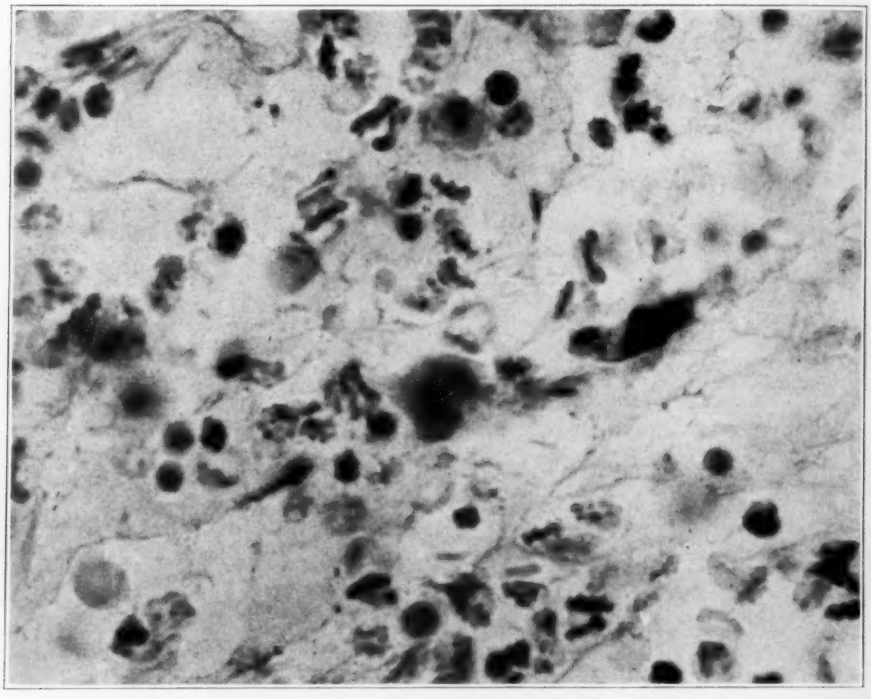

Fig. 2.—Bone marrow under high power magnification. The meshes of the reticulum contain degenerating red cells, two megakaryocytes and a few other cells, mostly lymphocytes.

Necropsy was limited to the examination of the organs mentioned.

Histologic Examination.—Bone Marrow: The marrow in the long bones, as well as in the ribs, showed enormous congestion with red cells, while between the vessels edema was prevalent. In addition to the endothelial cells lining the blood vessels, only scanty cells were present, most of which were polymorphonuclear leukocytes. There were also occasional large cells of the size of megakaryocytes, with one single oval or irregularly shaped nucleus. Many of the polymorphonuclears seemed to be degenerating. There were also a few reticulum cells with normally shaped nuclei. Myelocytes were found in places, but they were much less numerous than the polymorphonuclears (figs. 1 and 2).

Liver: There was no infiltration in the periportal fields, nor was there an unusual number of white cells in the sinuses of the liver. Many of the Kupffer cells showed evidence of red cell phagocytosis (fig. 3).

Spleen: The follicles were rather small. No secondary follicles were demonstrable, and the pulp was tremendously engorged. There was a slight hyperplasia of reticulum cells which occasionally formed distinct groups. Many other reticulum cells were swollen and loaded with hemosiderin. Some of these cells appeared in the distended sinuses (figs. 4 and 5).

Lungs: The lung was enormously engorged, and there was distinct stasis in many of the medium-sized blood vessels, with adjacent hemorrhagic infiltration of the alveoli and septums. Within such areas some of the bronchi were plugged by

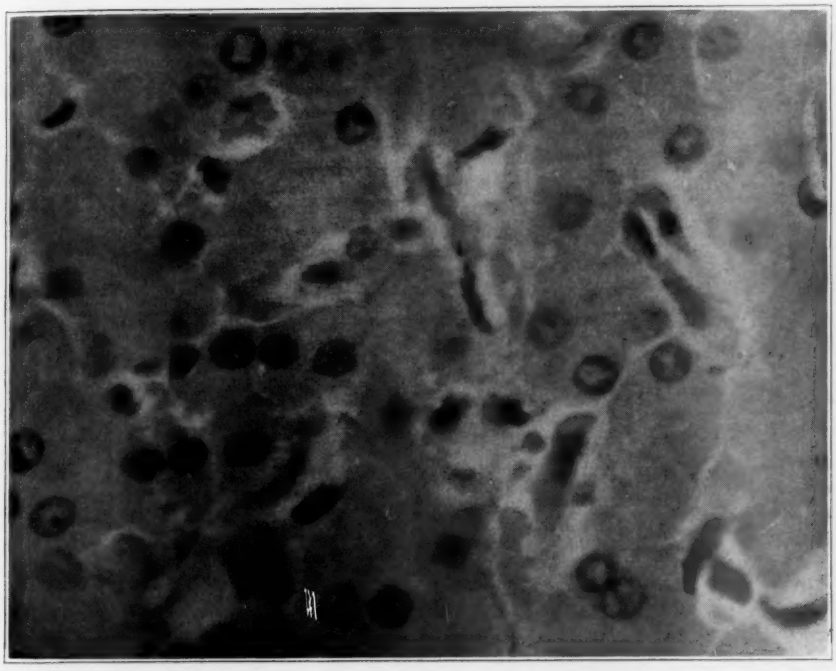

Fig. 3.—A section of the liver as seen under high power magnification. There are swollen Kupffer cells; no leukocytes are present in the sinuses.

cellular fibrinous exudate. These foci reached to the surface of the pleura; the pleura proper showed diffuse hemorrhagic infiltration and was covered with a fibrinous exudate. Other foci in the lung of similar hemorrhagic character showed a necrotic center in which cocci were demonstrable by Gram's stain.

This case differs in some respects from the classic picture of aplastic anemia in that: First, two remissions occurred before the fatal termination; second, there was a small amount of urobilin in the urine on June 9; third, hemosiderin was found in the liver and spleen; fourth, the bone marrow was a cranberry red; fifth, lymphoblasts were present in several of the blood smears, and sixth, adenopathy was present.

Although many observers stated in their discussion of this condition that the progress is rapidly and uninterruptedly downward until death occurs, remissions have been observed by some authors (Smith [22] and Benecke [26]). In Benecke's case, for example, there was a remission of several months. Hermann [6] stated that while it is true that in adults the disease is rapid in its course and invariably fatal, in children there appears to be a less acute form in which recovery is possible. To support his contention he referred to Parkinson's [5] and Benecke's [4] cases. It must be emphasized, however, that it is the consensus of most hema-

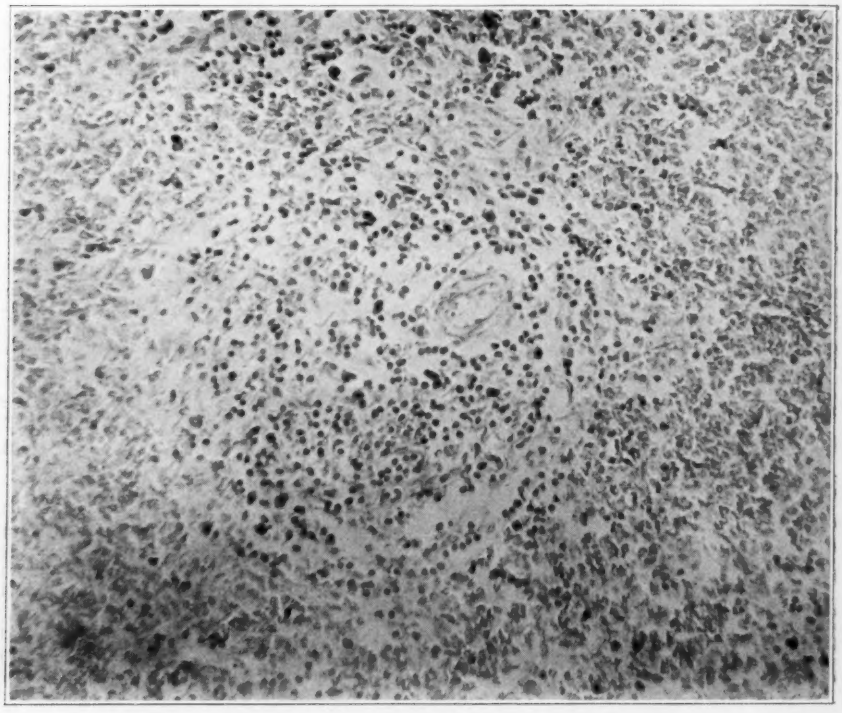

Fig. 4.—Photomicrograph of the spleen under low power magnification. Atrophic malpighian follicles are surrounded by engorged pulp.

tologists that recovery never takes place in a true case of aplastic anemia. A possible explanation of the remissions in the case presented here is that the factors producing the aplasia of the bone marrow were not constantly active, and that the destruction of the bone marrow occurred in waves.

The most generally accepted explanation is that the disease is due to a primary lesion of the bone marrow due to the action on it of some unknown toxic material, which results in a deficient production of red cells, polymorphonuclear leukocytes, myelocytes and platelets. Smith [22]

expressed the belief that in his case the toxin resulted from an attack of measles. In the case reported here it is likely that the severe infection of the upper respiratory tract initiated the disease; that the injection of toxin-antitoxin aggravated the condition, and that the subsidence of the infection with the aid of transfusions and the feeding of bone marrow brought about a remission. While I am loathe to ascribe the good results obtained to the feeding of bone marrow, it seems rather striking that, coincidentally with the administration of this substance, a definite and sustained increase in the red cells, white cells and platelets

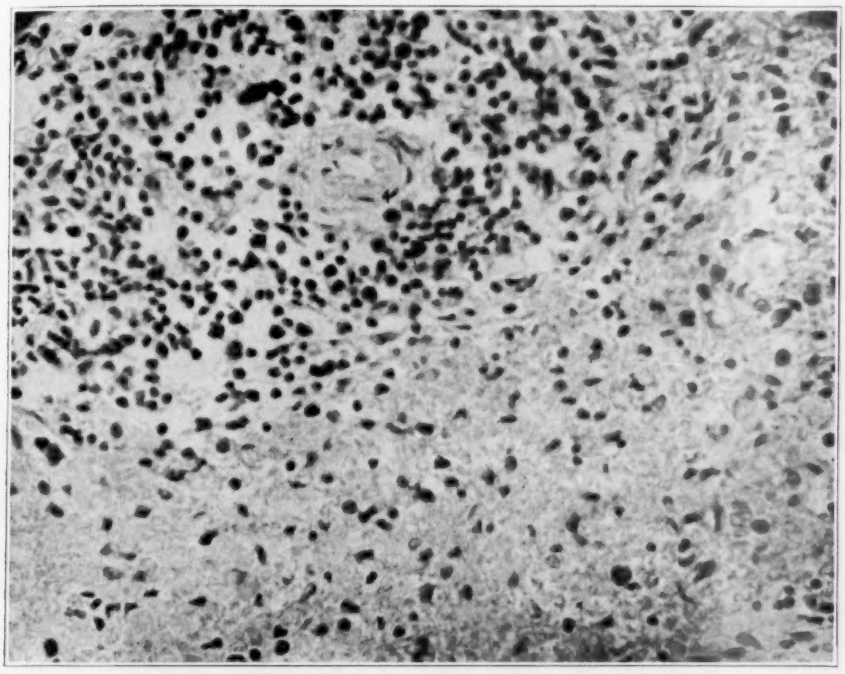

Fig. 5.—Section of the spleen under high power magnification. An atrophic follicle, with the adjacent pulp engorged, and scattered reticulum cells are seen.

occurred. The increase in these elements was even greater than when transfusions alone were given (accompanying table). That an acute infection may be the starting point of the disease has been observed by several authors (Smith [22]). It seems, however, that some other factor must be concerned in the pathogenesis, or many more cases of aplastic anemia would occur. It is possible that a congenital inferiority of the bone marrow is present from birth, and that an infection or toxic substance, which in a normal person would produce only mild and temporary changes in the bone marrow, is sufficient to bring about the severe, permanent and more or less widespread changes characteristic of aplastic

anemia. In fact, definite changes in the blood picture have been found in other members of a family in which this disease occurred. Bickel [30] studied the blood in four brothers and sisters of a patient with aplastic anemia and found evidences of injury to the bone marrow in all. Unfortunately, no studies were made of the blood of the parents of the child whose case is reported in this paper.

While it is true that at one time no distinction was made between pernicious anemia and aplastic anemia, it is now generally recognized that no relationship exists between the two. The evidence is definite that no increased destruction of red cells is present; for example, the skin is not icteric, the serum is light, and the fragility test gives normal results. The small amount of urobilinogen found in the urine in the case reported may well have resulted from the destruction of the trans-

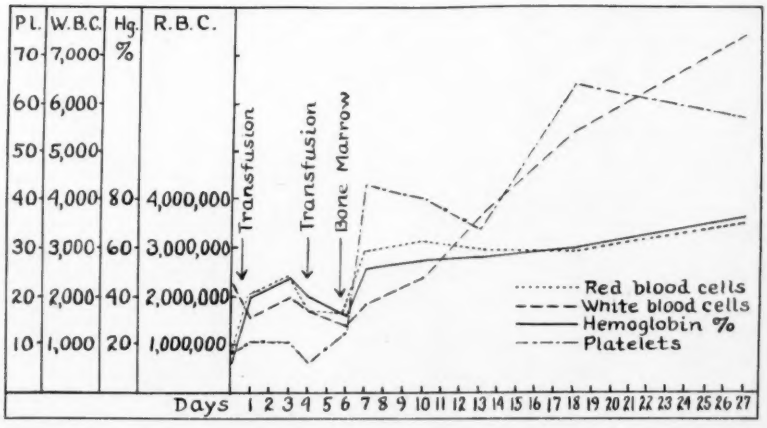

Fig. 6.—Hemogram made during the patient's first admission to the hospital.

fused blood and not from the destruction of the patient's red cells. As a matter of fact, it was found only once and in amounts insufficient for quantitative determination. The presence of hemosiderin found in the spleen of this patient is not without precedent (Smith,[22] Agnew [25] and Young [29]). A possible explanation is that the hemosiderin was derived from the transfused blood, or that iron was not sufficiently utilized in the formation of hemoglobin because of the markedly insufficient production of red blood cells and was therefore deposited after conversion in the spleen as hemosiderin. It has been recently shown that hemosiderosis of the spleen and liver follows transfusion of blood, and the amount of iron found in these organs is influenced by the size and frequency of the transfusions (Gladstone [31]).

30. Bickel: Wien. klin. Wchnschr. **42**:1286, 1929.

31. Gladstone, S. A.: Iron in the Liver and in the Spleen After Destruction of Blood and Transfusions, Am. J. Dis. Child. **44**:81 (July) 1932.

The most constant and striking pathologic change in this disease is the appearance of the bone marrow as a fatty yellow. The presence of a red bone marrow, however, should not lead one to discard the diagnosis of aplastic anemia until careful histologic study has been made. In this patient, while the bone marrow on gross examination appeared cranberry red, histologic examination revealed that this color was due to hemorrhage, and that there was an almost complete absence of cellular elements.

The only explanation for the presence of myeloblasts is that probably a panmyelophthisis is not present at the beginning of the disease, all portions of the bone marrow not being attacked by the toxin or other causative factor simultaneously; that some normal bone marrow is present at first, and that a general aplasia occurs as the disease progresses.

The presence of lymphoblasts in the blood and a generalized adenopathy have been reported by other observers. Benecke [26] described a case that showed enlargement of the lymph glands fourteen days before death. Swelling of the cervical, parotid, submaxillary and paratracheal glands was present in my patient four weeks before death. A possible explanation is that a severe injury to the bone marrow with a resulting disappearance of the granular leukocytes may lead to a secondary hyperplasia of the lymph nodes, because of an effort of the lymphatic system to assume the function of the aplastic bone marrow.

COMMENT

Etiology and Pathogenesis.—It is now generally conceded that aplastic anemia is a disease *sui generis* and is not a biologic variation of some form of primary or secondary anemia. Differences of opinion, however, still exist as to the pathogenesis. Hirschfeld,[18] Pappenheim,[3] Türck [14] and Naegeli [32] consider that the primary change is a disappearance of red cells, owing either to hemorrhage or to some toxin, and that regenerative changes do not occur because of a congenital or acquired deficiency in bone marrow. Frank [2] expressed the opinion that the aplastic anemia results from a primary aplasia of the marrow by some unexplained toxic action on the marrow itself, and that there is a simultaneous disappearance of erythrocytes, granulocytes and platelets. This theory explains his preference for the term panmyelophthisis.

A point against the theory of a primary increased destruction of red blood cells with a secondary aplasia is the fact that urobilinogen is practically never found in the urine; the serum is never yellowish, and bilirubinemia is never found.

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32. Naegeli, quoted by Baar and Stransky.[17]

Pathology.—The most characteristic finding is a sulphur yellow appearance of the bone marrow instead of the reddish appearance one would expect to find in severe anemia. This is due to a replacement of the normal marrow by ordinary fat tissue. In the case reported, the bone marrow was of a cranberry red appearance. Histologic examination showed, however, that the reddish appearance of the bone marrow was due, not to active regenerative processes, but to hemorrhage. As stated before, histologic examination revealed a total absence of nucleated red blood cells and myeloid elements. The only other cases reported in which the bone marrow was red were those of Babonneix and Tixier [9] and Muir.[24] In their cases, also, the color was due to hemorrhage into the bone marrow. As a general rule, the bone marrow is fatty only in older children; in young children the bone marrow may be pale, gray or rosy in color, but it is always poor in cells. In one of Kleinschmidt's cases [11] and in Benecke's case [26] the bone marrow was fatty. Hemosiderin deposits, when present, are found most often in the liver, but they have been noticed also in other organs, especially in the kidneys and spleen.

The disease is characterized by its rapidly and progressively fatal course; in no true case has the patient been known to recover. The two outstanding features of the disease are the severe anemia and the hemorrhagic diathesis, which manifests itself by hemoptysis, epistaxis and purpuric eruptions. Fever is usually present throughout the disease; the skin may or may not show pigmentation, depending on the rapidity of the course. In my patient, there was a distinct muddy, brown pigmentation of the skin. Cachexia and weakness are practically constant. Remissions do not occur as a rule. Necrotic processes of the mucous membranes of the mouth were encountered in some cases.

Blood Picture.—The blood picture is, of course, the main point of clinical diagnosis. There is a marked decrease in the hemoglobin content, with a diminution in the red blood cells to 1,000,000 or less; the hemoglobin is reduced to 10 or 15 per cent. The color index is approximately 1. Nucleated red blood cells are usually absent, although occasionally observers have found isolated normoblasts. Reticulocytes and polychromatophilic erythrocytes are absent. There is leukopenia with a marked reduction of the neutrophilic leukocytes and an almost complete absence of eosinophils. There is a relative increase in the lymphocytes. The differential count often shows the presence of only from 8 to 10 per cent polymorphonuclear cells, while the lymphocytes are frequently found to be 90 per cent or over. Thrombocytopenia is constant and is a feature of the disease. The coagulation time is normal, but the retraction of the clot is interfered with, and the bleeding time is prolonged. In addition to the absence of normoblasts and megaloblasts, myelocytes, myeloblasts or other forms of embryonic cells are

usually absent. The results of the fragility test are usually normal; Lucas, however, stated that the fragility of the red cells may be altered, owing to the inability of the bone marrow to produce new red cells.

The blood serum is water clear. There is no increase in bile pigments. Urobilinuria is absent, and there is no increase in the urobilin content of the stool. Although it is the opinion of most observers (Smith,[22] Baar and Stransky[17] and Abraham[33]) that the disease is clinically definite and the blood picture in most cases is conclusive, it has been my experience that the clinical symptoms and the blood picture may be encountered in the course of cases of aleukemic leukemia, in severe cases of essential thrombocytopenia and even in agranulocytosis. As is well known, secondary aplasia of the bone marrow occurs in some cases of leukemia. It is also possible that the so-called cases of essential thrombocytopenia and agranulocytosis result from a partial and selective aplasia of the bone marrow produced by some toxic factor,[34] the megakaryocytes being particularly involved in the former and the granulocytes in the latter disease.[35] As a general rule, it can be said that in the majority of cases the presence of typical pathologic changes in the bone marrow at necropsy is required for the final diagnosis.

Course.—The course of the disease is rapid, and it is usually fatal before four months have elapsed. In fact, some observers refuse to regard the case of a patient who lives longer than six months as a true case of aplastic anemia. This opinion, however, is not generally accepted; Abraham[33] stated that the disease may last from several months to a year and a half.

Treatment.—Up to the present no therapeutic measure has proved satisfactory in the treatment of this disease. Repeated transfusion is generally recommended, but it is, at best, only a palliative measure. In my patient, the administration of bone marrow, while it appeared to produce results in the first phase of the disease, failed to prevent a recurrence; it must, therefore, be considered of doubtful, if any, value.

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33. Abraham: Arch. f. Kinderh. **81**:1, 1915.
34. Hirschfeld, H.: Charité-Ann. **36**:573, 1912.
35. Greenwald, H. M.: Myelophthisis, J. Pediat. **3**:117 (July) 1933.

SEVERE PURPURA WITH GANGRENE OF THE LOWER EXTREMITY FOLLOWING SCARLET FEVER

RECOVERY AFTER AMPUTATION

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AND
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Gangrene of the extremities is one of the rare complications of scarlet fever. In a review of the literature, reports of only fifteen cases have been found, eleven of which were available for study. The first were by Lister[1] and Hudson[2] in 1858, followed later by those of Tungel,[3] Mayr,[4] Blaupain,[5] Kuster,[6] Holmes,[7] Chapin,[8] Pearson and Littlewood,[9] Eichhorst,[10] Buchan,[11] Hoyne,[12] Learmouth,[13] Schamberg and Kolmer,[14] and Sutherland.[15]

In the eleven cases reviewed, the age ranged between 3 and 40 years. They were about equally divided as to sex. The family history, when available, was negative for syphilis, tuberculosis and any hemorrhagic diathesis. The attack of scarlet fever in all cases was relatively mild, except that in Buchan's case, which was quite severe. Over half the cases

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1. Lister: Edinburgh M. J. **3**:893 (April) 1858.
2. Hudson, G.: Tr. Ohio M. Soc., 1858, p. 54.
3. Tungel: Virchows Arch. f. path. Anat. **16**:360, 1859.
4. Mayr: Jahrb. f. Kinderh. **3**:141, 1860.
5. Blaupain: Arch. méd. belge **9**:324, 1869.
6. Kuster, E.: Med.-chir. Centralbl. **17**:579, 1882; Ein chirurgisches Triennium, 1876-1878, Berlin, T. Fischer, 1882.
7. Holmes: System of Surgery, ed. 3, London, Longmans, 1883, vol. 1, p. 122.
8. Chapin: M. Age **11**:205, 1884.
9. Pearson and Littlewood: Lancet **2**:84 (July 10) 1897.
10. Eichhorst: Deutsches Arch. f. klin. Med. **70**:519, 1901.
11. Buchan: Lancet **2**:915 (Oct. 5) 1901.
12. Hoyne, A. L.: Raynaud's Disease, J. A. M. A. **45**:1725 (Nov. 13) 1915.
13. Learmouth: Canad. M. A. J. **15**:69 (Jan.) 1925.
14. Schamberg and Kolmer: Acute Infectious Diseases, ed. 2, Philadelphia, Lea & Febiger, 1928, p. 419.
15. Sutherland: Brit. J. Child. Dis. **27**:102 (April-June) 1930.

occurred with some other complication, five with nephritis (two with hematuria), three with some degree of cervical adenitis, one with otitis media and one with severe nosebleeds. In Hoyne's patients, following the acute phase of scarlet fever, measles, mumps, chickenpox, and whooping cough developed, after which there appeared symmetrical gangrene of both feet and legs, the tips of both ears, both cheeks and parts of both hands, terminating fatally with pneumonia. The date of onset of the gangrene varied from the seventh day of illness to nine months afterward. In most of them, however, it appeared from fourteen to twenty days after the beginning of the disease. In ten cases the gangrene was limited to the legs, in seven being unilateral and in three bilateral. In a single case the hands only were involved, and in one case both hands and both feet were affected. The mortality in the

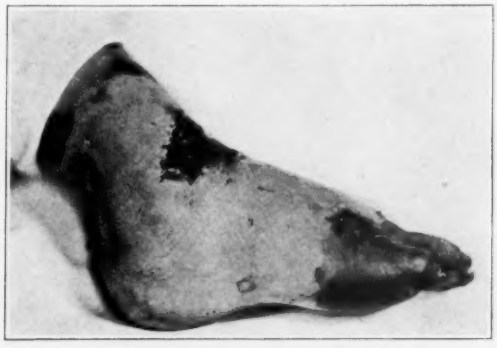

Fig. 1.—Spontaneous gangrene following scarlet fever.

cases reviewed has been close to 50 per cent. One patient recovered spontaneously after sloughing of the gangrenous portions of the toes and feet; four died without operation, and in six cases, one of which was bilateral, amputation was performed and all the patients recovered.

As to the pathologic changes in the gangrenous extremity, in four cases there was a thrombosis of the artery. One was embolic from vegetations on the mitral and aortic valves. In another case soft clots, not adherent to the wall of the artery and vein, were found after amputation. In two cases no evidence of either thrombosis or embolism could be found, and in three the pathologic changes were not recorded.

REPORT OF A CASE

History.—V. M., a white girl, aged 7 years, one of twin sisters, was admitted to the Presbyterian Hospital on July 6, 1931, with the history that on June 6 she became ill with scarlet fever. She had been taken to another hospital, where this diagnosis was confirmed. No complications developed until June 26, the twentieth day of her illness, when discoloration of the skin appeared on the dorsa of the feet,

the toes of the right foot, the lower lateral aspect of both thighs and the dorsa of both hands, and later in the subconjunctivae and tissues about the right eye. These areas had grown larger, the father said, especially those on the dorsum of the right foot. Convalescent serum had been given after the onset of the subcutaneous bleeding, but scarlet fever antitoxin had not been used.

The patient had had measles, whooping cough, chickenpox and convulsions at 1½ months of age; no hemorrhages were reported. The family history was negative for syphilis, tuberculosis or any hemorrhagic diathesis.

Fig. 2.—Microscopic section through the vessels of the gangrenous foot, showing a thrombophlebitis of the large vein. The lumen of the artery is open.

Examination.—On entrance the child was acutely ill, with a fever of 103.6 F. and a rapid small pulse. There were multiple bluish-black discolorations of the skin, the largest being on the right foot, covering the toes and extending back about 2 inches (5 cm.) on the plantar surface. Over the entire dorsum of the lower third of the leg the color was a reddish purple. No arterial pulsation could be made out in the foot. The other areas of discoloration, varying in size from 1 to 3 inches (2.5 to 7.6 cm.) in diameter, were located on the dorsum of the left foot, upper third of the left leg, lower lateral aspect of both thighs, dorsum of both hands, in the conjunctivae and about the right eye. In short, the foregoing picture, coupled with severe hemorrhagic gingivitis and tarry stools, gave one the impression of a severe fulminating type of purpura. Many of the dark areas were

covered with large bullae, which on bursting left a moist dark red surface. The examination gave otherwise negative results except for a slight cervical adenopathy and a soft systolic murmur over the whole of the precordium.

Laboratory Findings.—The hemoglobin content was 25 per cent. The red blood cells numbered 3,000,000; the white blood cells, 24,000; the platelets, 150,000. A smear showed 84 per cent polymorphonuclears, 8 per cent monocytes, 5 per cent lymphocytes, 1 per cent eosinophils and 2 per cent metamyelocytes. The blood calcium amounted to 9.7 mg. per hundred cubic centimeters. Urinalysis showed: blood, 4 plus, and albumin, 2 plus.

On the following day blood cultures were negative, and from the throat a green-forming streptococcus was isolated. The serum from the blisters showed no growth.

Course.—The patient was given 200 cc. of whole blood by direct transfusion on the day after admission, and this was followed by a chill and a temperature of about 106 F. The right foot and lower part of the leg became steadily darker, but no new hemorrhages appeared.

On the second day after admission (July 8) the line of demarcation became more clearly defined at about the junction of the middle and lower third of the leg (fig. 1). The temperature was 102.4 F., the pulse rate 120, the hemoglobin content 51 per cent, the red cell count 3,000,000, the white cell count 30,000, bleeding time five minutes and coagulation time five and a half minutes.

On July 9 a blood transfusion of 200 cc. was given by the direct method, followed again by a chill and high fever. The line of demarcation became still more marked, and the odor of the foot became very noticeable. On July 10 amputation was performed at the junction of the upper and middle thirds under ethyléne anesthesia, leaving the skin flaps wide open and the wound loosely packed with gauze. Except for a temporary trace of sugar and blood in the urine, the postoperative course was almost uneventful. The wound healed by secondary union and the temperature gradually returned to normal. The other areas of discoloration cleared slowly, some of them sloughing off, leaving clean ulcers which healed rapidly. The child was discharged from the hospital on the thirty-ninth day (August 14) with a hemoglobin content of 68 per cent and a healed wound.

Pathologic Examination.—Examination of the leg after amputation revealed no gross or microscopic evidence of block in the arteries supplying the gangrenous area. In the large veins, however, a recent thrombophlebitis was present (fig. 2). It seems quite probable in view of these findings that the subcutaneous hemorrhage occurred first, followed by a secondary septic thrombosis of the veins.

PNEUMOCOCCIC MENINGITIS IN THE NEWLY BORN

A CASE IN A TWO DAY OLD INFANT

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AND

PETER GANNONE, M.D.

PHILADELPHIA

Pneumococcic meningitis in the newly born is a rare disease, or at least it is infrequently reported.

Karplus,[1] in an exhaustive review of the literature, was able to discover only four cases up to 1927. Rueda[2] in 1927, Heinz[3] in 1928 and Uhr[4] in 1929 each reported one case. Because of the rarity of this condition, we feel justified in submitting the report of a case that came under our observation in April, 1932.

REPORT OF A CASE

Maternal History.—The mother, aged 21, had always been in good health. Her last menses were on July 2, 1931; up to March 3, 1932, her period of gestation was uneventful. On this day, however, she suddenly became ill with fever, chill, headache and backache. A diganosis of grip was made. She was ill for about two weeks, and had an obstinate cough and rhinitis, which persisted to a lesser degree up to the time of her discharge from the hospital. The Wassermann reaction and urinalysis were negative. Labor began on April 15, 1932, at 4 a. m. At about 4 p. m. she was delivered spontaneously of a 7 pound (3,200 Gm.) baby.

Child's History.—The infant at birth was cyanotic and showed some evidence of asphyxia. Artificial respiration was applied, and the child began to breathe within a few minutes. At no time did it show any of the signs of activity of a normal infant. Its cry was of a wailing type. When put to the breast for its first feedings, it made feeble attempts to nurse.

On the following day, April 16, it was observed that it made no effort to grasp the nipple, and that its cry had become weaker.

On April 17, the child began to have projectile vomiting. At about 10 p. m. it was desperately ill. At this time one of us was called in to see the infant. Physical examination revealed a practically moribund baby with a tense and slightly bulging fontanel. The eyeballs were pushed downward. The pupils were dilated and fixed. There was no rigidity of the neck. The temperature was

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1. Karplus, D.: Die Meningitis des Neugeborenen, Wien. klin. Wchnschr. **40**:250, 1927.

2. Rueda, P.: Pneumococcic Meningitis in a Fourteen Day Old Infant, Arch. latino-am. de pediat. **21**:765 (Oct.) 1927.

3. Heinz, H.: New England J. Med. **199**:218 (Aug. 2) 1928.

4. Uhr, J. S.: Pneumococcic Meningitis: Case in New Born Infant with Recovery, Arch. Pediat. **46**:121 (Feb.) 1929.

100 F., and at no time was it higher. The pulse and respirations were rapid. The remainder of the examination gave negative results. Lumbar puncture was performed, and a purulent fluid flowing at the rate of 72 drops per minute was obtained. The cell count was 1,129. A smear revealed many pus cells and many gram-positive diplococci. The culture showed pneumococci present. The infant died one hour following the spinal tap.

COMMENT

The interesting point as to the source of infection in this case may be raised. A careful check on all who came in contact with the infant revealed the mother as the possible origin. The next point arises as to whether the disease was acquired postnatally or in utero.

As the infant showed signs of abnormality from the moment of its birth and became progressively worse, and in view of the maternal history of illness shortly before term, we feel that the infection was acquired in utero.

CONGENITAL COMPLETE AURICULOVENTRICULAR HEART BLOCK

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Bradycardia during early childhood was mentioned first in 1896, by Schuster,[1] who reported a case of rheumatic fever in a child 4 years old who had transient bradycardia, with a rate of 35, the mechanism of which was unknown. It was not until 1908 that graphic proof of congenital auriculoventricular heart block was obtained.[2] In 1929, Yater [3] presented an exhaustive survey of the literature and tabulated the results in thirty cases, including one of his own. The auriculoventricular block was complete in twenty-two of these cases, the remainder showing varying degrees of partial block. Since Yater's publication, additional instances of congenital auriculoventricular heart block have been reported by Nicolson, Shulman and Green,[4] Leech,[5] Koenen [6] and Lampard.[7]

Two additional cases are presented, one of which is unique in view of the fact that the bradycardia was noted two months before birth, and was proved to be due to a complete auriculoventricular block two days after birth. In the second case, an interesting response to the atropine test was noted.

From the Sarah Morris Hospital and the Heart Station of the Michael Reese Hospital.

Aided by the Emil and Fanny Wedeles Fund for the Study of Diseases of the Heart and Circulation.

1. Schuster: Zur cardialen Bradycardie, Deutsche med. Wchnschr. **22**:484, 1896.

2. van den Heuvel, G. C. J.: Die ziekte van Stokes-Adams en een geval van aangeboren hartblok (Proefschrift aan de Ryks. Universität.), Gröningen, 1908.

3. Yater, W. M.: Congenital Heart Block, Am. J. Dis. Child. **38**:112 (July) 1929.

4. Nicolson, G.; Shulman, H. I., and Green, D. L.: Congenital Heart Block, Am. J. Dis. Child. **37**:580 (March) 1929.

5. Leech, Clifton B.: Congenital Heart Block, Am. J. Dis. Child. **39**:131 (Jan.) 1930.

6. Koenen, H. P. J.: Een geval van aangeborem compleet hartblock by ziekte van Roger, Nederl. tijdschr. geneesk. **74**:6000, 1930.

7. Lampard, M. E.: Heart Block Associated with Congenital Heart Disease, Arch. Dis. Childhood **3**:212, 1928.

REPORT OF CASES

CASE 1.—*History.*—C. C., a white male infant, was born on Nov. 20, 1927, by a normal, spontaneous delivery. For two months prior to birth, the obstetrician, Dr. M. L. Weinstein, was greatly concerned because the fetal heart persisted at the rate of from 44 to 48 per minute. After birth the heart continued at the same rate. The patient's 4 year old sister was living and well. The Wassermann and Kahn tests of the blood were negative for both father and mother.

Examination.—At birth, the patient's weight was 5 pounds, 13 ounces (2,669 Gm.), and he measured 48 cm. in length. A moderate, generalized cyanosis was present, more pronounced over the feet, hands and scrotum. There was no visible deformity of the body. The anterior fontanel was normal, that is, 1 inch (2.5 cm.)

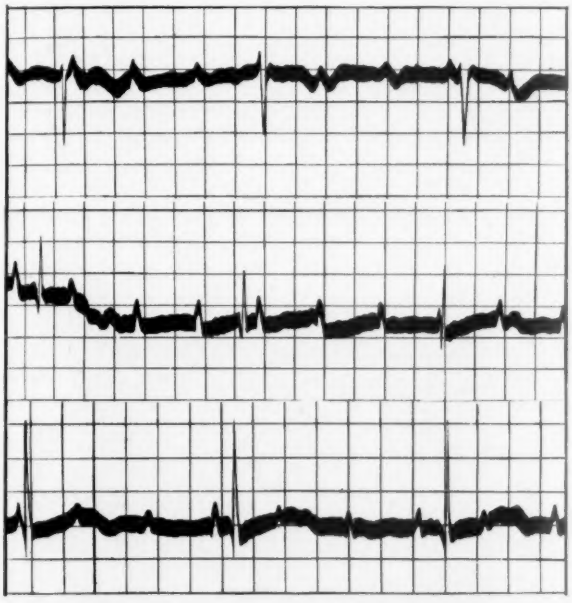

Fig. 1 (case 1).—Tracing of electrocardiogram.

in diameter. The cardiac dulness extended to the anterior axillary line on the left side and to the mammary line on the right. The area of dulness was so extensive that resonance could be obtained only over the infraclavicular regions, axillae and lower lateral portions of the chest. The heart rate was regular but, for the patient's age, decidedly slow—44 a minute. A soft systolic murmur could be heard over the base and midsternum. The abdomen was moderately distended and tympanitic. The liver was enlarged to one and one-half fingerbreadths below the costal arch. The spleen was also enlarged, extending to one and one-half fingerbreadths below the costal margin. There was no clubbing of the finger-tips or of the toes.

Laboratory Data.—The first electrocardiogram was taken when the infant was 2 days old; another was taken when he was 11 days old. Both showed a complete auriculoventicular block (fig. 1), with an auricular rate of 130 a minute and

a ventricular rate of 45. A roentgenogram (fig. 2) of the chest showed a markedly enlarged heart. Examination of the blood showed 90 per cent hemoglobin (Tallqvist), with 6,000,000 erythrocytes and 11,400 leukocytes. The Wassermann and Kahn reactions were negative. The urinalysis gave negative results.

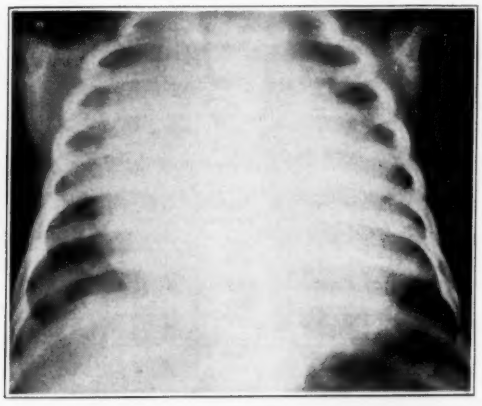

Fig. 2 (case 1).—Roentgenogram showing enormous cardiac enlargement.

Fig. 3 (case 1).—Gross specimen of the heart, showing a pronounced coarctation of the aorta. Note the intact interventricular septum.

Course.—During the first week, the cyanosis became pronounced when the child cried or ate. Expressed breast milk was fed by bottle for the first ten days. Thereafter a whole lactic acid milk mixture was given. The infant remained at the Sarah Morris Hospital until he was 20 days old. By this time the periods of

cyanosis were reduced in frequency and intensity. The infant's general appearance and color were fairly good, except during these cyanotic periods. At home he continued to gain steadily but slowly until the third month, when the periods of cyanosis again became more pronounced. The child died on February 6, at the age of 2 months and 17 days.

Autopsy.—The heart (fig. 3) was greatly enlarged; before the pericardial cavity was opened, the greatest transverse diameter measured 7 cm. The pericardial cavity was free from fluid and adhesions. The visceral and parietal pericardium were smooth and glistening. There was a slight increase in the size of each auricle. The right ventricle was greatly dilated, and its musculature was hypertrophied. The endocardium of the right ventricle was prominently thickened. There was no defect in the tricuspid or in the pulmonary valves. The interventricular septum was intact. The pulmonary circulation showed no deviation from normal. The cavity of the left ventricle was also markedly dilated, and the endocardium was prominently thickened. The musculature was hypertrophied and of a deep purplish brown, and had a slightly firmer feel than usual. The mitral and aortic valves showed no lesion. A probe could be passed with difficulty through the foramen ovale, but this opening was probably not functional. The same was true of the ductus arteriosus. The arch of the aorta was somewhat more than moderately dilated proximally, and in the area where the innominate artery and the left common carotid and subclavian arteries were given off, there was a slight narrowing, but between the point of exit of the left subclavian and the point of entrance of the ductus arteriosus, there was a pronounced narrowing of the aorta.

The anatomic diagnosis was coarctation of the aorta; hypertrophy and dilatation of the heart, and pressure atelectasis of the lower lobes of both lungs. Unfortunately, during a period of reconstruction in the building where the pathologic examination was made, the specimen was lost before a histologic study could be undertaken.

CASE 2.—*History.*—W. S., a white boy, aged 6 years, was brought to the outpatient department of the Michael Reese Hospital for the first time on Oct. 2, 1929. The mother's reason for seeking medical advice was a rash on the boy's hands and trunk, which was promptly recognized as typical scabies.

The parents disclosed the fact that when the child was 1 year old they were informed that a heart murmur had been heard. They had observed that the child's lips became "bluish" at times, during cold weather or while swimming. The birth history was irrelevant. He had chickenpox at 3 years and measles at 4. There was no history of any other illness or of infectious disease.

Examination.—A general physical examination attracted attention to the slow heart rate—54 a minute. The cardiac area was slightly enlarged, the apex extending to 1 cm. outside of the nipple line in the left fifth interspace. The right cardiac border was 3 cm. to the right of the midsternal line. A long systolic murmur could be heard over the entire precordium, maximal over the left fourth interspace to the left of the sternum and transmitted to the neck. There was no cyanosis or clubbing of the finger-tips. No other congenital defect could be detected. The patient was well developed and well nourished. His pupils were equal and reacted to light and accommodation. The pharynx and tonsils were normal. The teeth were normal and in excellent condition. The lungs were clear. The edge of the liver was barely palpable. The spleen and kidneys were not palpable. The genitalia were normal. All reflexes were normal.

Laboratory Data.—Examination of the blood showed 80 per cent of hemoglobin (Tallqvist), 4,750,000 erythrocytes and 9,600 leukocytes, with a differential count

of 50 per cent polymorphonuclears. The Wassermann and Kahn reactions were negative. The Mantoux and Pirquet tests were likewise negative. The urinalyses showed nothing important. The blood pressure was 122 systolic and 75 diastolic. An electrocardiogram (fig. 4), taken on Oct. 7, showed a complete auriculoventricular block, with an auricular rate of 108 and a ventricular rate of 52 a minute. A teleoroentgenogram showed a transverse diameter of the heart of 10.9 cm., with

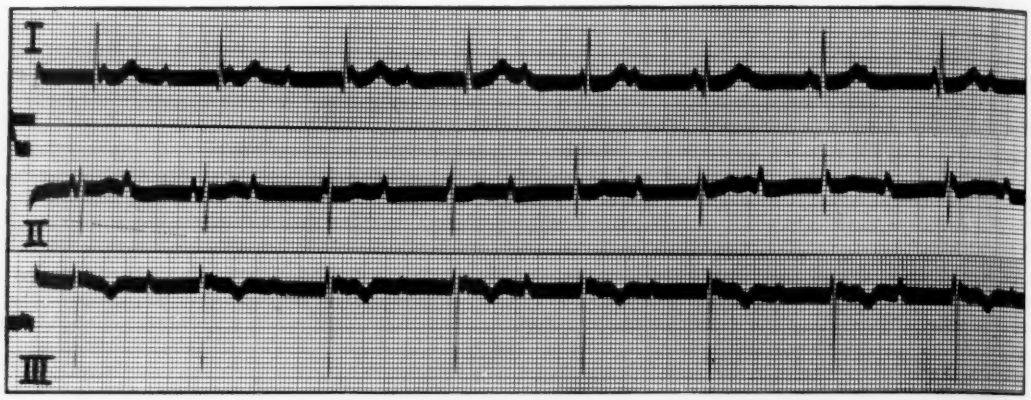

Fig. 4 (case 2).—Note the difference in P P intervals usually characteristic of heart block; i. e., the intervals which include a Q R S complex are shorter.

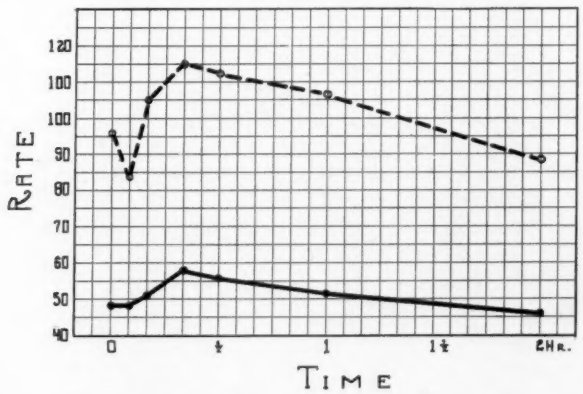

Fig. 5 (case 2).—The effect of atropine on the auricular and ventricular rates measured from serial cardiograms. Hypodermic injection of 1/50 grain (0.0013 Gm.) atropine sulphate given at *O* (time). The broken line indicates auricular rate; the straight line, ventricular rate.

a transverse diameter of the chest of 18.4 cm. The contour of the heart was somewhat globular.

A clinical diagnosis of congenital heart disease with complete heart block was made.

Course.—Observation of this patient has been continued at the outpatient department for three years. During this period the boy has shown no symptoms referable

to his cardiac derangement. His general condition remains good; he participates in the usual daily activities of normal children. Electrocardiograms have been taken at various intervals. All tracings show a persistence of the complete auriculoventricular block, with the ventricular rate varying from 48 to 52, and the auricular rate ranging from 98 to 108.

Effect of Epinephrine Hydrochloride and Atropine Sulphate.—Epinephrine hydrochloride produced an increase in both the auricular and the ventricular rates. The electrocardiogram taken before the injection of epinephrine hydrochloride showed an auricular rate of 98 and a ventricular rate of 50. Fifteen minutes after the hypodermic injection of 0.5 cc. of a 1:1,000 solution of epinephrine hydrochloride, the auricular rate was increased to 108, and the ventricular rate, to 63.

Five minutes after the hypodermic injection of $\frac{1}{50}$ grain (0.0013 Gm.) of atropine sulphate, the auricular rate dropped from 96 to 79; the ventricular rate of 48 remained unchanged (fig. 5). The rates soon increased to a maximum of 115 for the auricles and 58 for the ventricles at the end of twenty minutes. A gradual slowing then occurred, so that after two hours the rates were slightly less than at the outset, dropping to 94 for the auricles and 46 for the ventricles. Complete auriculoventricular block persisted in all records. A similar transient slowing of the auricles had been noted previously—the auricular rate dropping from 100 to 86 within fifteen minutes after the hypodermic injection of $\frac{1}{50}$ grain of atropine sulphate.

COMMENT

The complete heart block in case 1 was unquestionably a congenital condition. In only two instances was there any prenatal suggestion of heart block. In the first case of White, Eustis and Kerr,[8] the fetal heart rate was found to be irregular eight hours before birth, and in the case reported by Yater,[3] the fetal heart beat was recognized to be slower than the mother's pulse for two weeks before birth.

Congenital heart block is almost always associated with congenital heart lesions. The co-existence of a congenital heart lesion with heart block was mentioned in all except four of the reported cases. Until recently it had usually been assumed that the block was either due to, or associated with, a deficiency of the interventricular septum. Patent interventricular septum was diagnosed clinically in sixteen instances.

Postmortem studies were made in only two of the proved cases. The case reported by Wilson and Grant[9] presents the only definite proof of an interventricular septal defect; the patient was a child of 14 months with partial heart block of congenital origin. Necropsy disclosed absence of the interventricular septum. The conducting system followed an abnormal course from a well developed auriculoventricular node in the interauricular septum near the coronary sinus. The authors found a muscular prominence on the posterior ventricular

8. White, P. D.; Eustis, R. S., and Kerr, W. J.: Congenital Heart Block, Am. J. Dis. Child. **22**:299 (Sept.) 1921.

9. Wilson, J. G., and Grant, R. T.: A Case of Congenital Malformation of the Heart in an Infant Associated with Partial Heart Block, Heart **12**:295, 1926.

wall, commencing at the interauricular septum, behind the aortic orifice, lying between the mitral and tricuspid valves and breaking into trabeculae toward the apex. This prominence was regarded by them as the rudiment of the posterior horn of the interventricular septum. Two main strands of nodal tissue accompanied by blood vessels passed through dense fibrous tissue from the auriculoventricular node to this muscular prominence, where they seemed to appear as a single narrow band penetrated and surrounded by fibrous tissue. This band was followed with difficulty but seemed to spread out into definite Purkinje fibers after passing down the muscular prominence and giving off one branch to the right anterior portion of the ventricle.

In the other case in which postmortem examination was made, no gross defect of the interventricular septum was noted, but a lesion affecting the auriculoventricular node and bundle was found. In this connection it is interesting to note the case of a 5 year old child with heart block, reported by Armstrong and Mönckeberg,[10] which showed a small primary tumor localized in the auriculoventricular node. In Yater's case of an infant who lived only eighteen days, necropsy revealed developmental anomalies of the head and neck, transposition of all viscera and great vessels except the ventricles of the heart, patent ductus arteriosus, patent foramen ovale and a small patency in the interventricular septum. Histologic examination showed a complete separation of the node from the bundle. The auriculoventricular node was completely separated at its anterior end into a large portion above and on the right side of the central fibrous body and a smaller portion below. The upper portion faded out, but the lower, smaller portion became larger, and undoubtedly was the auriculoventricular bundle. The right bundle branch could not be found. The sino-auricular node was located in the opposite side of the heart from the auriculoventricular node. In this case the impulse from the sino-auricular node, after reaching the auriculoventricular node, was unable to pass on to the auriculoventricular bundle on account of the complete anatomic separation of the node from the bundle. The Q R S T, or ventricular complex of the electrocardiogram was of the supraventricular form, indicating that the independently originated ventricular impulse arose high in the bundle of His.

Case 1 in this report presents another example of congenital heart block which is not due to a patent interventricular septum. It is therefore concluded that in those cases in which a clinical diagnosis of patent interventricular septum was made, the heart block must be explained on

10. Armstrong, H., and Mönckeberg, J. G.: Herzblock, bedingt durch primären Herztumor, bei einem 5 jährigen Kinde, Deutsches Arch. f. klin. Med. **102:** 143, 1911.

some basis other than the associated septal defect. This view is strengthened by the fact that there are numerous instances in which the septum is entirely absent and the auriculoventricular node and bundle of His are functionally normal. As stated by Leech,[5] "the evidence offered by the accumulated cases suggests that congenital heart block is invariably due to a lesion sufficiently high above the bifurcation of the bundle of His to allow the production of normal ventricular complexes in the electrocardiogram."

The effect of atropine sulphate in case 2 was extremely interesting. A brief preliminary retardation of the auricles, followed by a transitory increase in the auricular and ventricular rates, was noted. Lewis[11] stated that an initial slowing may occur with hypodermic injections of atropine. The action of atropine in cases of congenital heart block has been mentioned in only nine cases. Fleming and Stevenson[12] observed that $\frac{1}{200}$ grain (0.00033 Gm.) of atropine sulphate caused an increase in the rate of the auricles and ventricles. Leech showed that $\frac{1}{150}$ grain (0.00043 Gm.) of atropine stimulated both auricles and ventricles to increased activity. In the remaining reports the ventricular rate was not changed by this drug. In one case, the auricles alone were retarded.

The effect of epinephrine in congenital heart block has been recorded by a number of observers with results similar to those reported here.

SUMMARY

Two cases of congenital heart disease with complete auriculoventricular heart block are presented. The first is unique in view of the fact that the bradycardia was noted two months before birth, and was proved by electrocardiogram to be due to a complete auriculoventricular block two days after birth. Autopsy revealed a greatly enlarged heart with coarctation of the aorta—a finding which has not been observed in the cases heretofore reported. There was no defect in the interventricular septum. In the second case an interesting response to the atropine test was obtained, showing a preliminary retardation of the auricles followed by a transitory acceleration of both auricles and ventricles.

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11. Lewis, Thomas: The Mechanism and Graphic Registration of the Heart Beat, ed. 3, London, Shaw & Sons, 1925.

12. Fleming, G. B., and Stevenson, M. M.: Heart Block Associated with Congenital Malformation of the Heart, Arch. Dis. Childhood **3**:221, 1928.

Progress in Pediatrics

ACUTE ENTERITIS IN INFANTS AND IN YOUNG CHILDREN

I. BACTERIOLOGIC STUDIES

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CINCINNATI

I. BACTERIOLOGIC METHODS, MORPHOLOGY AND CULTURAL CHARACTERISTICS OF STREPTOCOCCUS MICRO-APOIKIA

A review of the literature dealing with the bacteriologic observations in "acute intestinal intoxication of infants," "epidemics of enteritis in infants," "summer diarrhea in children" or "acute toxic gastro-enteritis in infants" reveals that more emphasis has been placed on the isolation of Bacillus dysenteriae and closely allied micro-organisms from the stools of such patients than on the finding of any other single bacterium. Johnston, Brown and Kaake,[1] in studying sixty-seven infants with acute intestinal intoxication, isolated twenty-one strains of B. dysenteriae, twenty-six of Bacillus schmittzii, four of Bacillus asiaticus and three of Bacillus paratyphosus-B. In their study of twenty-nine children, from 2 to 12 years of age, they isolated seventeen strains of B. dysenteriae, three of B. schmittzii and one of B. paratyphosus-B.

Kendall [2] in 1915 expressed the view that different types of bacteria may elicit the same general clinical response in children. In 1910 he isolated B. dysenteriae from the stools in 75 per cent of fifty-two cases of "summer diarrhea in children." In 1911 similar micro-organisms were isolated in 12.3 per cent of one hundred and forty-six such cases. In addition, although the clinical picture in the cases was the same in 1911 as in 1910 it was observed that seventy-eight of these one hundred and forty-six children harbored streptococci in large numbers, and in many instances sequelae caused by streptococci, such as septicemia,

From the Children's Hospital Research Foundation and the Department of Pediatrics, College of Medicine, University of Cincinnati.

1. Johnston, M. M.; Brown, A., and Kaake, M. J.: Canad. Pub. Health J. **22**:441, 1931.

2. Kendall, A. I.: Boston M. & S. J. **172**:851, 1915.

otitis media and nephritis, developed. He also noted at necropsy that the lesions in which streptococci were present in considerable numbers differed from the lesions observed at necropsy when B. dysenteriae was seemingly the etiologic agent. In 1912 Bacillus aerogenes-capsulatus, and in 1913 another bacillus belonging to the encapsulated group of bacilli, predominated. He placed no unusual emphasis on the presence of the streptococci. Kendall's observation that there is a shifting of the dominant organism from year to year is important. It coincides with our own experience. As a matter of fact, the streptococcus to be described was not present in preponderating numbers in an epidemic of enteritis occurring in 1932.

Jörgensen [3] attributed to Bacillus welchii the etiologic rôle in acute toxic gastro-enteritis in children. Other studies, too numerous to quote, have been made on the bacteriology of the intestinal tract in diarrheal diseases.

During the past three years increasing evidence has accumulated in the Children's Hospital of Cincinnati and the department of pediatrics at the Cincinnati General Hospital of the importance of certain types of streptococci as agents of disease (Cooper [4]). The relation of these streptococci to an epidemic of enteritis in forty-six infants and children is being reported in the following communications. During the course of this work a technic for cultivation has been developed which will be detailed in this article, together with a report of the morphology of these micro-organisms and their reaction in the fermentation of sugars.

EXPERIMENTAL METHODS

Culture Mediums.—The following mediums were used:

Minced Brain Broth: This medium is quite similar to the dextrose brain broth used by Rosenow. Its main difference consists in the preparation of the brain. All blood clots and meninges are removed from fresh calf brain, which is then run through a fine meat grinder so that it is practically a thick emulsion. A layer of about 1½ inches (3.8 cm.) of this minced brain is deposited by means of a large glass tube in the bottom of large test tubes, 18 cm. by 22 mm. Broth prepared as follows is then added in quantities of 25 cc. to each tube: 8 Gm. of bacto dehydrated nutrient broth medium, 8 Gm. of sodium chloride, 2 Gm. of chemically pure dextrose, and 10 cc. of Andrade's indicator, all dissolved in 1,000 cc. of distilled water. The 2 Gm. of chemically pure dextrose and 10 cc. of Andrade's indicator are added last to the solution. Finally two or three small pieces of crushed marble are added to each tube. Sterilization is carried out for twenty minutes at 20 pounds' pressure. In this medium the emulsified brain is in a compact mass in the bottom of each tube, and it appears that this favors the growth of these streptococci. The final p_H is 6.9.

3. Jörgensen, G.: Jahrb. f. Kinderh. **111**:63, 1925.

4. Cooper, Merlin L.: (*a*) J. Med. **10**:175, 1929; (*b*) The Cause of Poliomyelitis, abstr. Am. J. Dis. Child. **42**:702 (Sept.) 1931.

Semisolid Medium: This medium is prepared by adding 4 gm. of agar per liter of Bacto brain heart infusion broth.

Blood Agar: This medium is prepared by adding 6 per cent of fresh normal rabbit blood to sterile Bacto brain veal agar. The final p_H is 74.

Carbohydrate Broth Mediums: To Bacto nutrient broth is added 0.5 per cent of the desired carbohydrate and 5 per cent of a 0.1 per cent solution of phenolsulphonphthalein in nutrient broth. The final p_H was adjusted to 7.4. The carbohydrates used were dextrose, saccharose, mannite, maltose, raffinose, salicin, lactose and inulin. These carbohydrate mediums were dispensed in 4 cc quantities in small test tubes, 100 by 12 mm., and sterilized for fifteen minutes at 15 pounds' pressure. The cultures to be tested were first grown in blood broth for from eighteen to twenty-four hours, and 0.25 cc. quantities of such cultures were inoculated into each of the tubes of sugar broth.

The Endo medium was freshly prepared Bacto Endo's agar.

Anaerobic Apparatus.—The anaerobic apparatus was an improvement over a similar method used with good results in 1919. It consisted of a large pyrex desiccator connected, through a manometer and three-way stopcock, to a Cenco Hyvac Pump and tank of pure hydrogen. In the center of the jar, near the top, was a heating unit consisting of several turns of nichrome wire, B. and S. gage 28, which was wound and evenly spaced around platinized asbestos and surrounded by fine meshed copper gauze. After the Petri dishes had been placed in this jar it was sealed and evacuated at least four successive times, with the introduction of hydrogen after each evacuation, to slightly less than atmospheric pressure. The coil of nichrome wire was then heated to the glowing point for ten minutes by means of a rheostat-controlled direct current motor generator.

CHARACTERISTICS OF GROWTH

It has been found in this laboratory that these small-colony, green-producing streptococci from stools grow best at times anaerobically and at other times under reduced oxygen tension. The routine for cultivation which has been worked out in this study is as follows: The culture is made as quickly as possible after obtaining the material to be studied. The specimen is streaked thoroughly over the surfaces of two plates of blood agar and two Endo plates. One of the plates of blood agar is placed in the anaerobic jar. In addition a small portion of the specimen is placed in a large tube of the mixed brain broth. All cultures are incubated at 37.5 C. and are studied after twenty-four hours. The blood plate which is incubated in the anaerobic jar shows the color of deoxygenated hemoglobin and must be left exposed to the air for at least half an hour so that it may regain its normal blood agar appearance. The plates are then examined for all tiny colonies, regardless of whether or not there is a green area about them, since the green area is frequently absent from the initial colonies. The only definite characteristic of these colonies is their minuteness. All tiny colonies are picked for isolation and study and are transferred to tubes of the minced brain broth and incubated. The initial brain broth culture is streaked onto the surfaces of freshly prepared plates of blood agar, some of which

are incubated in the anaerobic jar. The following day the plates are examined for all types of colonies but especially for minute colonies surrounded by narrow faint green areas which are frequently present on this first subculture. Any such colonies are transferred to sections of a blood plate to determine purity and to study the characteristics of the colony. If pure, they are picked to semisolid mediums in which they live for about two months. These streptococci seldom grow out aerobically from the semisolid medium if transferred directly to aerobic blood agar; they must first be transferred to the brain broth and secondly to the surface of blood agar. They usually die after two or three days on the surface of blood agar but will live for about ten days in the brain broth medium. The Endo plates are examined carefully for any dysenteriae-like colonies, and if such colonies are seen they are studied and identified.

The chief characteristic of this streptococcus is, as stated, its formation of unusually small colonies. The production of a green color on mediums is secondary in importance, and, furthermore, this and the morphology of the micro-organism do not seem to differentiate it from other streptococci. For this reason it is suggested that the term "Streptococcus micro-apoikia" (small-colony) be employed to distinguish this group of streptococci from others, and that suitable terms be added to connote their peculiar pathogenic properties. For example, the micro-organism described in this article could be designated as "Streptococcus micro-apoikia enteritidis."

MORPHOLOGIC CONSIDERATIONS

Morphologically these streptococci vary considerably, depending on the medium in which they are cultivated and on their age. In stained smears of the intestinal contents they are seen as gram-positive diplococci, slightly elongated in the axis extending at right angles to their plane of juxtaposition, or, occasionally, as short chains of small diplococci. From the colonies on blood agar they stain as small gram-positive diplococci. It is in the initial or subsequent early cultures of brain broth that they generally assume their most bizarre forms. In such cultures one frequently sees marked pleomorphism. In some chains the cocci vary in size and shape between large elongated club forms and very minute cells which are barely visible as a continuation of the chain. There is just as much variation in the staining of these cells with Gram's stain as there is in their morphology. This is particularly true of the tiny forms in which some cells stained gram-positive and others gram-negative. There is less variation in the large cells. The majority stain gram-positive, some gram-negative and a few neither definitely positive nor negative.

As an example of the manner in which these streptococci grow, strain Ro may be cited. This, which was the most pleomorphic of any strain obtained from blood or stool, was isolated directly from the blood of a patient shortly before death. In brain broth it demonstrated unusual pleomorphism, individual adjacent cells having striking variation in size, shape and staining reaction (fig. 1). It was difficult to cultivate, and grew slowly and sparsely in the brain broth. It failed to grow on solid mediums except in the presence of blood and then only slowly and poorly. Yet this culture, as reported in the subsequent articles, was one of the most virulent and satisfactory for the production of typical pathologic changes in the intestinal tracts of monkeys and rabbits.

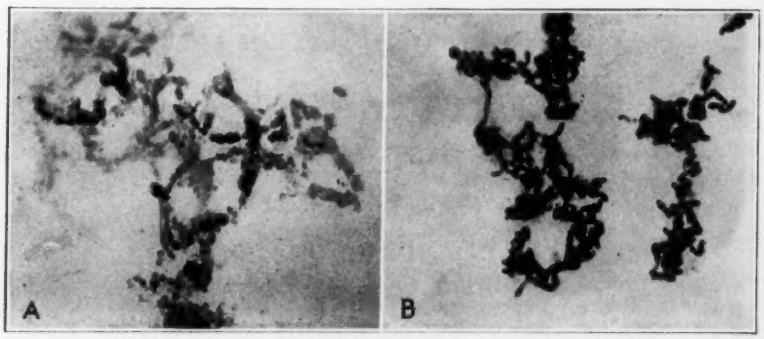


Fig. 1.—Gram stains of Streptococci micro-apoikia. *A*, long chains showing variations in the size of the cells and gram-staining in the same chain; *B*, pleomorphism resembling diphtheroid morphology.

COLONY CHARACTERISTICS

The colonies of these streptococci were studied by means of a Bausch and Lomb wide field binocular microscope. In general, the characteristics were definite. The majority of the cultures produced colonies on blood agar which were very small, smooth, raised and granular, with an oval surface. The edges of the colonies were generally quite regular and even, at times appearing to be sharply elevated. At other times this edge seemed to be not only sharply elevated but also slightly rolled back on itself. These variations may be attributable to slight differences in the moistness of the surface of the blood agar. The center of the colony was usually depressed. The green area around the colonies was a narrow band, evenly surrounding them and extending into the medium under the colonies to a depth approximately equal to their extensions laterally beyond their edges. The red blood cells in the area within the limits of the green band were slightly darker than the red blood cells in the normal medium beyond the green area. Some strains of

these streptococci produced colonies in the green area of which part of the red blood cells became hemolyzed after forty-eight hours. Other strains never showed any hemolysis even when cultivated on a portion of the same plate of blood agar with a strain that did show slight hemolysis. This slow and slight hemolysis generally developed after prolonged incubation. Earlier experiments had shown that hemolysis was more likely to occur if the initial hydrogen ion concentration of the medium was about p_H 7.0. If the initial p_H was about 7.5, this slight hemolysis was much less likely to occur. Further work is in progress in relation to the influence of mediums on the growth of "Streptococcus micro-apoikia.

FERMENTATIONS OF CARBOHYDRATES

It is generally considered that with streptococci determinations of carbohydrate fermentations are unsatisfactory. Reports indicate that

TABLE 1.—*Comparison of the Carbohydrate Fermentations of Streptococci from the Throat and Stool Cultures of the Same Patient*

Patient	Source of Streptococci	Dextrose	Lactose	Saccharose	Inulin	Maltose	Raffinose	Salicin	Mannite
Be	Throat	+	+	+	+	+	+	+	—
	Stool	+	+	+	+	—	+	—	+
Po	Throat	+	+	+	+	+	+	—	—
	Stool	+	+	—	+	+	—	—	+
Le	Throat	+	+	+	+	+	—	+	—
	Stool	+	+	+	+	+	+	+	+
On	Throat	+	+	+	+	+	+	—	—
	Stool	+	+	+	+	+	+	+	+
Ka	Throat	+	+	+	+	+	+	—	—
	Stool	+	+	+	+	+	+	+	+
Ke	Throat	+	+	+	—	+	—	—	—
	Stool	+	+	+	—	+	+	+	+

results vary with repetition and that different strains apparently of the same streptococcus do not ferment the various carbohydrates uniformly. However, the need for any aid for differentiating Streptococcus micro-apoikia from other streptococci is so great that no possibilities can be neglected, and, therefore, extensive tests with eight carbohydrates were made. These experiments were carried out with cultures isolated from several sources as follows: from patients at necropsy, from rabbits at necropsy, from stools of monkeys which had received injections, from throats of patients with enteritis and from throats of patients not having enteritis.

Table 1 gives a comparison of fermentations of carbohydrates by Streptococcus micro-apoikia isolated from the throat and stool cultures of the same patients with enteritis. These results show that the streptococci from the throat and stool of the same patient frequently fermented the majority of the sugars in a strikingly similar way. If we compare the fermentative powers of the streptococci of the various

patients, we again see a marked similarity; such a comparison seemingly indicates that what appeared to be an occasional discrepancy when comparing streptococci from the throat and stool of the same patient might really be only a difference due to recent environmental changes. In one instance, K, the streptococci from both the throat and the stool, failed to ferment inulin which was fermented by the streptococci from both the throat and the stool of all the other patients.

TABLE 2.—*Carbohydrate Fermentation with Streptococci Recovered at Necropsy from Patients with Enteritis*

Patient	Source of Streptococci	Dextrose	Lactose	Saccharose	Inulin	Maltose	Raffinose	Salicin	Mannite
Wa	Stomach	+	+	+	+	+	—	+	+
	Duodenum	+	+	+	+	+	+	+	+
	Middle ileum	+	+	+	+	+	+	—	+
	Terminal ileum	+	+	+	+	+	+	—	+
	Cecum	+	+	+	+	+	+	—	+
	Ascending colon	+	+	+	+	+	+	—	+
	Transverse colon	+	+	+	+	+	+	—	+
Ru	Sigmoid	+	+	+	—	+	+	+	—
	Rectum	+	+	—	+	—	+	—	—
Ro	Blood	+	+	+	—	+	+	+	—
Bo	Spinal fluid	+	+	+	+	+	+	—	—

TABLE 3.—*Comparison of Carbohydrate Fermentations by Streptococci Isolated from Patients with Enteritis and as Reisolated at Necropsy from Rabbits which Received Injections*

Patient	Rabbit	Dextrose	Lactose	Saccharose	Inulin	Maltose	Raffinose	Salicin	Mannite
Ro	...	+	+	+	—	+	+	+	—
	272	+	+	+	—	+	—	+	+
	306	+	+	+	—	+	—	+	—
	360	+	+	+	—	+	+	+	—
Ba	...	+	+	+	+	+	+	—	—
	139	+	+	+	+	+	—	+	—
Be	...	+	+	+	+	—	+	—	+
	138	+	+	—	+	+	—	+	+
Cl	...	+	+	+	+	+	+	+	+
	263	+	—	+	+	+	+	+	—
He	...	+	+	+	+	+	—	+	—
	239	+	+	+	+	+	—	+	+

In table 2 are seen the carbohydrate fermentations of eleven strains of these streptococci isolated from patients at the time of necropsy. In this table, which lists the seven strains isolated from various sources in the body of one patient, there is a striking similarity in the way the cultures affect the several carbohydrates.

In experiments with animals it was important, of course, to know whether the strains of streptococci recovered from animals which had received injections were identical with those injected. Therefore the carbohydrate fermentation of many of these streptococci was determined

before and after passage through animals in both rabbits and monkeys. In table 3 are seen the data regarding the rabbits which received injections. In general there is a noticeable similarity. In forty-four of fifty-six comparisons the streptococci recovered from the animals had the same carbohydrate fermentations as did the streptococci originally injected. However, the most satisfactory proof in this connection was the subsequent injection of these cultures into animals, and this method was relied on largely for such evidence.

In table 4 is shown a comparison of the carbohydrate fermentations of streptococci recovered from the stools of monkeys which had received

TABLE 4.—*Carbohydrate Fermentation with Streptococci from Stools of Monkeys which Received Injections and from Their Small Intestine at Necropsy*

	Dextrose	Lactose	Saccharose	Inulin	Maltose	Raffinose	Salicin	Mannite
Strain injected: Ro.....	+	+	+	—	+	+	+	—
Monkey 1								
Stool 6.....	+	+	+	+	+	+	—	—
Small intestine.....	+	+	+	—	+	+	—	—
Monkey 2								
Duodenum.....	+	+	+	+	—	—	+	—
Small intestine.....	+	+	+	+	—	—	+	—
Monkey 3								
Stool 4.....	+	+	+	+	+	+	—	—
Stool 6.....	+	—	+	+	—	—	—	—
Monkey 4								
Stool 6.....	+	+	+	+	+	—	+	—
Stool 14.....	+	+	+	+	+	—	+	—
Small intestine.....	+	+	+	—	+	—	+	—
Monkey 6								
Blood.....	—	—	+	+	+	+	+	—
Small intestine.....	+	+	+	+	+	—	+	—
Monkey 7								
Stool 11.....	+	+	+	+	+	+	—	—
Duodenum.....	+	+	+	+	+	+	+	—
Small intestine.....	+	—	+	+	+	+	+	—

injections and also from their small intestines at necropsy with those of the culture injected. In general there is a close agreement, especially as manifested in saccharose, mannite and dextrose, there being only one discrepancy among forty-two comparisons. The greatest disagreement is seen in the fermentations of inulin, since there are only two agreements in fourteen comparisons. These inulin-fermenting strains were not soluble in bile. Several of these cultures were subsequently injected into other animals and produced the typical pathologic changes in the small intestine.

In table 5 are seen the marked similarities between the carbohydrate fermentations of sixteen strains of the streptococci isolated from the stools of patients with enteritis. Many such cultures were used in experiments with animals and proved to be the type capable of producing the characteristic pathologic changes in the intestines.

Table 6 presents a summary of the results of carbohydrate fermentation. All cultures have been grouped according to their sources, and the groups are listed in the order of their decreasing fermenting power. It is seen from this table that the streptococci from the stools of patients with enteritis were the most active in the fermentation of carbohydrates; those from the necropsy cultures of such patients were next and were

TABLE 5.—*Carbohydrate Fermentations of Streptococci from Stools of Patients with Acute Enteritis*

Patient	Dextrose	Lactose	Saccharose	Inulin	Maltose	Raffinose	Salicin	Mannite
Ke	+	+	+	+	+	—	+	+
Ri	+	+	+	+	+	+	+	+
Ba	+	+	+	+	+	+	—	—
Be	+	+	+	+	—	+	—	+
Ga	+	+	+	+	+	+	+	+
Po	+	+	—	+	+	—	—	+
Pr	+	+	+	+	+	+	+	+
Pa	+	+	—	+	+	—	+	+
La	+	+	+	+	+	+	+	+
Le	+	+	+	+	+	+	+	+
On	+	+	+	+	+	+	+	+
Cl	+	+	+	+	+	+	+	+
Sm	+	+	—	+	+	—	+	+
He	+	+	+	+	+	—	+	—
Ka	+	+	+	+	+	+	+	+
Ku	+	+	+	+	+	+	—	—

TABLE 6.—*Summary of Carbohydrate Fermentations*

Source of Streptococci	Number of Strains	Dextrose, per Cent	Lactose, per Cent	Saccharose, per Cent	Inulin, per Cent	Maltose, per Cent	Raffinose, per Cent	Salicin, per Cent	Mannite, per Cent
Stools of patients with enteritis	16	100	100	81	100	94	69	75	81
Necropsy cultures of patients with enteritis	14	93	93	86	79	86	86	29	65
Stools of monkeys given injections	14	93	79	79	93	93	43	57	14
Throats of patients with enteritis	15	93	93	100	63	93	60	34	7
Necropsy cultures of monkeys given injections	41	80	73	78	73	71	51	61	34
Necropsy culture of rabbits given injections	43	86	66	81	54	93	56	30	30
Throats of patients without enteritis	13	80	30	70	60	60	60	30	0

followed in the order of decreasing activity by streptococci isolated from the stools of monkeys which had received injections, throats of patients with enteritis, postmortem cultures of rabbits which had received injections, and streptococci from the throats of patients who did not have enteritis. Judging from these results with one hundred and fifty-six strains one may conclude that the streptococci from the stools and postmortem cultures of patients with enteritis are the most active fermenters, those from the animals which received injections and from throats of patients with enteritis are the next most active, while those

from the throats of patients with conditions in no way related to enteritis are the least active.

These results do not, of course, show that the streptococci from the throat and stool of the same patient are identical, but they are suggestive of a close relationship. This is of more significance in view, first, of previous observations (Cooper [4a]) that similar streptococci are frequently found in pure culture in the pharynx of patients during the first six hours following the onset of an acute cold, and secondly, of the fact that, as shown in a succeeding article of this series, 74 per cent of patients with acute enteritis had an acute infection of the upper respiratory tract just preceding, and in most cases at the time of, the onset of the enteritis.

It is evident that although there is a definite suggestion of similarity in the carbohydrate fermentations of Streptococcus micro-apoikia there is, at the present time, no possibility of determining the virulence of this organism by cultural, morphologic or fermentation characteristics. The only means of determining the virulence is by inoculation of animals. Data have accumulated—and will be presented later—which demonstrate by animal experimentation that these streptococci isolated at necropsy from various parts of the bodies of patients with enteritis and those isolated from the intestinal tract and stools of such patients are in all probability identical. Some of the streptococci isolated from the throats of patients with enteritis and patients with early acute "colds" also have the ability to produce similar intestinal lesions and death in experimental animals.

SOLUBILITY IN BILE

All the cultures were tested for their solubility in bile with 0.1 cc. of ox bile to 1 cc. of broth culture. All the cultures were insoluble in bile except two strains from monkeys which received injections; these were questionably so. One of these was isolated from the stool, the other from the lower part of the small intestine.

SUMMARY

1. Bacteriologic methods are presented which were used in the isolation of streptococci from 65 per cent of forty-six infants and children with acute enteritis.

2. Morphologic and cultural characteristics of these streptococci alone were found to be insufficient for identification.

3. Marked similarities in the fermentations of carbohydrate were noted in the streptococci isolated from the involved intestinal tracts of patients at necropsy, from the stools of patients, from the throats of

patients and from the intestinal tracts of animals which had received injections.

4. All the cultures were insoluble in bile with the exception of two, which were questionably so.

5. For the reasons stated it is suggested that the term Streptococcus micro-apoikia (small colony) be employed to designate this group of micro-organisms, and that the term Streptococcus micro-apoikia enteritidis be employed to designate the strain responsible for the production of enteritis in the patients who were the subjects of this study.

Pediatric Biographies

TOBIAS KATZ
1652-1729

JOHN RUHRÄH, M.D.
BALTIMORE

Apparently not a great deal is known about the details of the life of Tobias Katz, one of the Jewish physicians of the seventeenth and eighteenth centuries. What is known was embodied in two articles by A. Levinson, in 1917.[1]

Tobias was born in 1652 at Metz, where his father had settled after being driven out of Russia by the Cossacks, and he lived in Metz until the death of his father; then he went to Krakow, where he studied medicine. This move was only the first in a long series of travels which led to Tobias mastering nine languages and acquiring a knowledge of the life of peoples in many lands. Later he studied in Frankfort and afterward in Padua, where he took his degree in medicine. In Adrianople, he wrote his book "Maaseh Tuviah, The Work of Tobias," which was published in Venice. In his wanderings he finally came to Constantinople, where he is said to have been court physician to five sultans. His last journey was to Jerusalem, where he died and was buried.

His book, which is in Hebrew, is one of those encyclopedias that were popular in his time, and treat of all sorts of things of heaven and earth, that is, religion, philosophy, astronomy, geology and chemistry, but chiefly of medicine. He had read widely and included in his book the usual medical beliefs of his time, which were mainly copied from the ancients and the Arabians. He compared the body to a house. The hair is the roof; the eyes are the windows; the mouth, the door; the lungs, the upper ventilated story; the stomach, liver and spleen, the middle story, in which the baker has his kitchen and in which the cellar (spleen) is located; the kidneys, the water reservoir; the lower intestines, the water closet, and the feet, the foundation.

Tobias knew of and believed in contagious diseases, and added facts and fancies of his own to the knowledge of others. Under the heading,

1. Levinson, A.: A Medical Cyclopedist of the Seventeenth Century, Bull. Soc. M. Hist. Chicago **2**:27, 1917; The Pediatric Section of a Medical Cyclopedia of the Seventeenth Century, ibid. **2**:110, 1917.

"The Fruit of the Womb," which Levinson translated, he gives sixteen short pediatric chapters. He had the current superstition that colostrum was not only bad for the child but was poisonous, an idea which was greatly elaborated on by Ezekiel de Castro, another Jewish physician, in his "Il Colostro," which has already been considered. He thought that the cradle should be away from a window or a candle lest the child, looking in that direction, develop strabismus. He ascribed poor nourishment to witchcraft or to worms. The former might act through "a look and by an evil eye or from the poisonous breath of a menstruating

TOBIAS KATZ
1652–1729
(Courtesy of Dr. Harry Friedenwald)

woman or sometimes even from the mother herself." Passages from the Bible could be used to counteract this evil influence, or various remedies could be used. Among them he mentioned: "The placenta of a first child dispels all witchcraft, thus doing away with emaciation due to magic. The placenta is pulverized and given to the baby to drink either in some liquid or togther with its mother's milk." This suggestion is like much of the advertising matter on organotherapy that is sent through the mail today.

The foregoing idea is particularly interesting, for the theory that witchcraft was a cause of children's diseases, although current at the time, rarely got into medical books. It was a vagary more popular with lawyers and theologians than with physicians.

The following extracts from Levinson's translations will give some idea of Katz' style:

CHAPTER III.—Chapter III speaks of children poor in flesh on account of worms in the skin.

At times children are thin and meager in flesh on account of very small creatures that breed deep in the skin. In French, they are called Krinunish, in Spanish, Lus Ispanicus (and in German, Die Mitesser).

The symptoms are the following: The child nurses a great deal but it is not satisfied. Its skin becomes like a fur coat, and it is poor in flesh.

The remedy is to bring the child to a bath house or to put it in a bath tub full of water and make it sweat. Then anoint the skin of the child's body with honey so that the heads of the worms will come out. They will look like the sprouting of black hair. Then run over them a piece of bread crumb or a razor so the heads will come off and they will be destroyed.

Another method is to take ash water in which the manure of young roosters has been cooked. Put this in a bathtub and put the child in with water up to his neck to sweat. Then with a little anointing of honey, the heads of the worms will come out. These should be destroyed with a razor or a piece of bread, as explained above. At times the worms persist in multiplying themselves. Then vigorous treatment is necessary.

CHAPTER IV.—Chapter IV speaks of children poor in flesh from some other causes.

Behold children are poorly nourished because of many reasons, sometimes on account of bad milk. Then it is necessary to improve the mother's milk. At times it is because of the wetnurse, then it is necessary to change the nurse; at times on account of constipated bowels, then it is necessary to use laxatives; sometimes, too, on account of worms in the intestine, then it is necessary to drive them out. If it is due to too much heat then it is necessary to use cooling remedies. The same is true of other causes and of other remedies, each of which finds its proper place in different chapters of my book.

CHAPTER V.—Chapter V speaks of a clogging up of the nostrils, due to some discharge or a thick exudate.

At times there goes down from the head into the spongy bone of the nose a thick exudate which causes the stuffing up of the nostrils and bad breath. It is then necessary to use melting remedies.

The remedy is almond oil, 1 drachm; muranah oil, 2 or 3 drops applied to the nose and nostrils; or flax should be dipped in the extract of batah twisted like a wig; or 2 or 3 drops of mintah grass should be taken and made into a wig for the nostrils.

CHAPTER VII.—Chapter VII speaks of sleeplessness in children. Its causes and remedy.

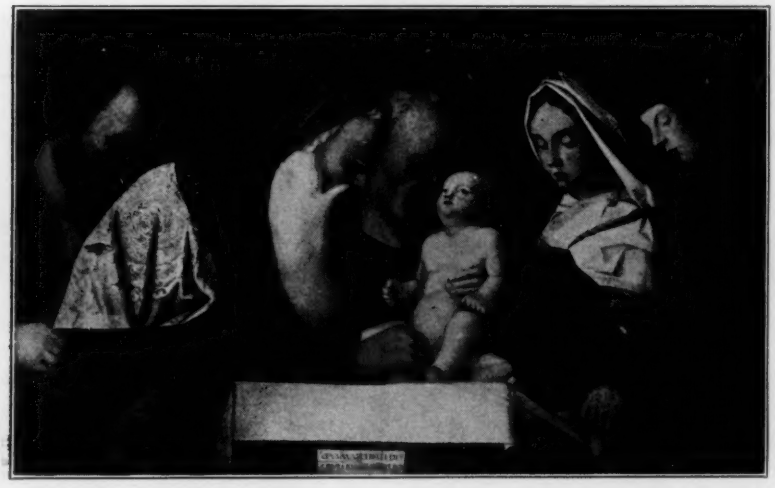
It is the nature of little children to sleep. This is because of the great amount of humor in them. At times, however, the child is not natural and does not sleep at all neither by day nor by night. This is caused by vapors that go up to the head. The remedy is to revert to the cause and to use evacuating remedies. For instance, one should take syrup of ramnu or chicory, or mannah or cassia or other remedies that produce light laxation and that cleanse the inside. Then they [the children] should be washed in water of Lorber-blätter, or Kinus leaves, but no grass should be used that will put the child to sleep, because of the danger of such. God save us from all mistakes. Amen!

Pediatrics in Art

CIRCUMCISION

JOHN RUHRÄH, M.D.
BALTIMORE

There are many pictures showing the circumcision of the Infant Jesus, as it was a favorite topic with the early painters and with some of the later ones. Every kind of an operation is shown by one artist or another, and there are a great variety of poses and of assistance. The



"La circoncisione" by Marco Belli

mohel is almost always represented with a long flowing beard, a great handicap for a surgeon of any kind. The interesting thing about the picture, "La circoncisione" by Marco Belli, which is in the Pinacoteca de' Concordi at Rovigo, is the absence of any evidence of surgical instruments and the position of the child, which for the operation could not have been worse. So one can believe that Belli had never witnessed a circumcision and relied entirely on his imagination. The swaddling band has been removed but is still on the left leg, and the woman at the child's side is holding the part which has been unwound. It is of finer cloth than was customary. In many instances the binder was over 30 feet long, and the arms and legs were bound first and then the entire body.

News and Comment

GENERAL

Congress of French Pediatric Association.—The Eighth Congress of the French Pediatric Association will be held in Paris on July 9 to 11, 1934.

UNIVERSITY NEWS

Dr. G. Vidal Jordana has been named professor of pediatrics to the Faculty of the University of Barcelona.

DEATHS

Dr. Alfredo Larguia of Buenos Aires, a well known Argentine pediatrician, died recently.

Dr. Tadashi Suzuki, professor of pediatrics at the Imperial University of Kyoto, died recently at the early age of 51. Dr. Suzuki was not only head of the department in his university, but he was likewise editor in chief of the *Oriental Journal of Diseases of Children.* He was an outstanding pediatrician and one of the best known of the Japanese scientists in this line. His death at such an early age is to be greatly regretted.

Abstracts from Current Literature

Pathology, Bacteriology and Biochemistry

ALLEGED ANTAGONISM BETWEEN DIGITALIS AND DIPHTHERIA TOXIN. HARRY GOLD, MARGARET M. KLUMPP and THOMAS D. SLAGLE, Am. J. M. Sc. **185**:509 (April) 1933.

Experiments were carried out on sixty-six cats. The results showed that digitalis does not afford protection against poisoning by diphtheria toxin in these animals. The assumption is drawn that the same is probably true in man. The summary contains the following statement: Results obtained with diphtheria toxin in guinea-pigs have been used as a basis for the statement that "in acute pneumonia digitalis could be regarded as a life-saving remedy." This assumption is unwarranted and has received no support from systematic statistical studies which show that the routine use of digitalis in pneumonia does not lessen the mortality.

HENSKE, Omaha.

IMMUNOLOGIC BEHAVIOR OF THE SECOND PROTEIN (LIVETIN) OF THE HEN'S EGG YOLK. T. H. JUKES and H. D. KAY, J. Exper. Med. **56**:469 (Oct.) 1932.

By means of anaphylactic, precipitin and complement-fixation tests, the authors show the close similarity between, if not the actual identity of, the livetin of egg yolk and the serum globulin of the common fowl. They suggest the possibility of the transmission of immunity from maternal serum to the offspring by this means. A brief review of work along similar lines with milk and egg white is given. Mention is made of the fact that the caseins of various milks are closely related, but that the whey proteins are species specific, and that each contains a protein which is probably identical with the serum globulin of the species from which the milk is obtained.

LUECKE, Dallas.

TOTAL AND FIXED CALCIUM IN PATHOLOGIC TISSUES. JOSEPH WEILL, Compt. rend. Soc. de biol. **109**:125 (April 13) 1932.

The amounts of total and fixed calcium per hundred cubic centimeters of blood were determined in four cases of latent tetany, thirteen of chronic rheumatism and eight of atrophic myotonia. The findings were:

Latent tetany	Total calcium	7.3 to 8.5 mg.
	Fixed calmium	7.0 to 8.0 mg.
Chronic rheumatism	Total calcium	11.7 mg.
	Fixed calcium	7.0 mg.
Myotonia atrophica	Total calcium lowered in 6 cases and normal in 2.	
	Fixed calcium lowered in 1 case and elevated in 7.	

WAHL, Cleveland.

RESPIRATORY EQUIVALENT IN CHILDREN. E. PÜSCHEL, Monatschr. f. Kinderh. **57**:349, 1933.

The respiratory equivalent is defined as: $\frac{\text{minute volume}}{\text{calculated oxygen need} \times 10}$ in cubic centimeters. The calculated oxygen need is obtained from the formula: $\frac{\text{calculated metabolism}}{7.07}$.

Püschel's investigations show that the respiratory equivalent for children is independent of age and sex and about the same as that for adults. More work

is necessary to define the variations more definitely. The equivalent is lower following the consumption of food than during fasting.

The author's findings confirm those of Speck, namely, that the consumption of oxygen, the respiratory rate and the depth of respiration are increased with the ingestion of food.

GERSTLEY, Chicago.

DETERMINATION OF CHOLESTEROL IN SMALL QUANTITIES OF BLOOD. H. FESTEN, Nederl. tijdschr. v. geneesk. **77**:997 (March 4) 1933.

A method is described for the quantitative determination of cholesterol in 0.4 cc. of blood. This method is based on the reaction of Liebermann and Burchard.

VAN CREVELD, Amsterdam, The Netherlands.

Nutrition

THE NUTRITIVE VALUE AND EFFICIENCY OF MINERALIZED MILK. A. R. KEMMERER, C. A. ELVEHJEM, E. B. HART and J. M. FARGO, Am. J. Physiol. **102**:319 (Nov.) 1932.

Rats reared from weaning on whole cow's milk mineralized with iron, copper and manganese grew from 60 to 200 Gm. in thirty-six days, a gain similar to that made by rats on an ordinary ration. Similar results were obtained with pigs. Thus the nutritive value and efficiency of whole cow's milk were demonstrated by direct feeding after the deficiencies in the milk were corrected by the addition of inorganic supplements.

NOURSE, Cleveland.

NUTRITION FOR SUPERIOR GROWTH. I. NEWTON KUGELMASS, Arch. Pediat. **49**:713 (Nov.) 1932.

Kugelmass discusses the essential principles of adequate nutrition and reviews the subject from the standpoint of requirements for energy, food and vitamins. The article does not lend itself to abstraction.

WADDELL, JR., University, Va.

POWDERED CITRIC ACID MILK IN INFANT FEEDING. HAROLD D. LYNCH, Arch. Pediat. **49**:763 (Nov.) 1932.

Lynch compares a small series of babies fed powdered citric acid milk with a similar series fed powdered whole milk. The addition of citric acid appeared neither to raise nor to lower the value of powdered milk as a food for infants. Milk altered by physical means seemed to require less alteration by chemical means as an aid to digestion, in that the optimum quantity of dehydrated citric acid used in fresh whole milk formulas proved to be excessive in the powdered milk preparation. The author doubts that acid is needed in dry milk used as a routine feeding for infants, but he feels that acid milks have an important place in the feeding of infants.

WADDELL, JR., University, Va.

JUVENILE OBESITY. HUGO R. RONY, Endocrinology **16**:601 (Nov.-Dec.) 1932.

Since there is a wide difference of opinion as to the rôle of endocrine disturbance in the etiology of obesity, Rony studied fifty unselected cases in children ranging in age from 7 to 18 years, whose excess weight varied between 25 and 128 per cent of the normal average weight.

The study included investigation of the history, clinical examination, measurement of growth and of sexual and mental development, determination of the basal metabolism and of the sugar tolerance and roentgen examination of the sella turcica.

Some of the findings were as follows: In twenty-four cases the father, the mother or both were obese. In thirty-two cases obesity had been present since infancy. In twenty-four cases there was retarded sexual development. The sella turcica was in general normal in outline. There was a tendency to low basal

metabolic rates. Sugar tolerance was normal in twenty-one cases, high in seventeen and low in eight. In fourteen cases there was evidence of mental or nervous deficiency. Only six children showed no abnormalities.

An attempt was made to group the children according to evidence of hypofunction or hyperfunction of the pituitary gland, the thymus gland and the gonads. But since the deviations from normal were in both directions, the conclusion is that there is a relationship between endocrine anomalies and obesity, but it is not of an etiologic nature.

The literature on the experimental production of obesity and of other abnormalities noted in this series is quoted in an effort to prove the existence of a hypothetic center, probably of hypothalamic origin, disturbance of which would produce all the changes noted.

JACOBSEN, Buffalo.

QUANTITATIVE VARIATIONS IN VITAMIN A CONTENT OF BUTTER FAT. G. S. FRAPS and RAY TREICHLER, Indust. & Engin. Chem. **24**:1079, 1932.

Butter fat from cows on a ration of cotton seed meal, hulls, sorghum ensilage and pasturage contained an average of 33 units of vitamin A per gram. Cows fed silage without access to pasture gave an average of 4 units, while cows fed cotton seed meal and hulls alone produced butter fat containing 2 units per gram. Only a small fraction of the vitamin A of the feed appeared in the butter fat.

KUGELMASS, New York.

VITAMIN A AND PROTEIN CONTENT OF VARIOUS FISH MEALS. L. A. MAYNARD, R. C. BENDER and C. M. MCCAY, J. Agric. Research **44**:591, 1932.

Commercial fish meals which differ in origin and in method of manufacture may also differ greatly in nutritive value, as shown by the experimental feeding of rats. Vacuum-dried whitefish meal is a good source of vitamin A, in contrast to steam-dried and flame-dried menhaden meals, which are lacking in this vitamin. Vacuum-dried whitefish meal is also superior to steam-dried menhaden meal, and the latter is superior to flame-dried menhaden meal, in regard to protein efficiency for growth. The results suggest that the differences in the methods of heating are at least partially responsible for the nutritive differences found.

KUGELMASS, New York.

BASAL METABOLIC RATES OF VEGETARIANS. GLEN WAKEHAM and LOUIS O. HENSEN, J. Biol. Chem. **97**:155 (July) 1932.

The average basal metabolic rate of twenty persons who had been vegetarians all their lives was found to be 11 per cent below the DuBois normal rate. None of these subjects was a vegetarian in the strictest sense, however, as milk was used freely, and eggs were used occasionally. A period of from six to eight years is required to produce this effect. The average rate of twenty persons who had been vegetarians for from one to five years was 1 per cent below normal, and that of fourteen persons who had been vegetarians for from six to ten years was 6.5 per cent below. Occasional lapses on the part of habitual vegetarians have no effect on the average basal metabolic rate. KUGELMASS, New York.

A REVIEW OF CERTAIN CLINICAL ASPECTS OF NUTRITION. JULIAN D. BOYD, J. Pediat. **2**:226 (Feb.) 1933.

The recent developments in the field of nutrition are summarized, and the clinical significance of each of the vitamins is discussed briefly. The rôles of iodine, iron and calcium in the diet are considered separately. The essentials of an adequate diet, as well as the deficiencies most frequently seen, are also discussed, and there are numerous references to the latest literature on nutrition.

LEMASTER, Evanston, Ill.

BIOPHYSIOLOGICAL APPETIZERS IN THE NUTRITION OF THE CHILD. GEORGE DOW SCOTT, M. J. & Rec. **136**:449 (Dec. 7) 1932.

One of the most useful biologic stimulants of the pediatrician is water, for it exerts a decided action on the hunger mechanism of the stomach. The fruit juices have an added attraction in that they contain both vitamins and salts. In the child, water inhibits the contractions of the stomach but it may prompt these contractions through stimulation of the nerve endings in the mucosa of the stomach by mechanical pressure, by osmosis or by changing the chemical equilibrium of the contents of the stomach. The child's body requires three things from the outside world: food, oxygen and water. A child, ill or well, ingests just as much fluid as the body craves, and should not receive more. Sufficient water, however, is an essential constituent of the cytoplasm of the cell. The cell may hunger, thirst or become overfatigued, and it may cry out for food, water or rest before one knows that it is in need of this.

WILLIAMSON, New Orleans.

THE ANTIRACHITIC POTENCY OF THE MILK OF HUMAN MOTHERS FED PREVIOUSLY ON VITAMIN D MILK OF THE COW. JOHN W. M. BUNKER, ROBERT S. HARRIS and RICHARD S. EUSTIS, New England J. Med. **208**:313 (Feb. 9) 1933.

According to Hess, Lewis, MacLeod and Thomas, vitamin D cow's milk, when fed directly to infants, will cure or prevent rickets. A group of mothers was given 24 ounces (680.3 cc.) of vitamin D milk daily in addition to the regular diet, but no cod liver oil, viosterol or other antirachitic supplement was used. A control group received no vitamin D milk. It was found that the breast milk of mothers to whom antirachitic supplements to a mixed diet had not previously been given did not heal rickets in rats when 20 cc. of milk per animal per day was fed for eight days. The breast milk of mothers to whom 24 ounces of vitamin D milk had been given daily for two weeks as an antirachitic supplement to an otherwise adequate diet was found to have an antirachitic potency equivalent to 1 rat unit in 136 cc. of breast milk (17 cc. per rat per day for eight days).

The authors conclude that the antirachitic potency of human breast milk can be augmented in a simple and acceptable manner by including vitamin D milk in the diet of the mother during lactation.

GENGENBACH, Denver.

SEASONAL VARIATION OF AVERAGE GROWTH IN WEIGHT OF ELEMENTARY SCHOOL CHILDREN. CARROLL E. PALMER, Pub. Health Rep. **48**:211 (March 3) 1933.

Approximately 2,500 native-born white children attending the elementary schools of Hagerstown, Md., were weighed monthly during the school years from September, 1923, to May, 1928. The maximum increase in weight occurred during the fall months, the intermediate increase during the winter and the minimum increase during the spring. During the summer period the weight increased about the same amount as in February and March. During the sixth and seventh years of life there was no consistent difference between the rate of growth of boys and that of girls. During the eighth and ninth years boys grew slightly faster than girls. In the spring of the tenth year the rates for girls became higher than the rates for boys; they remained higher for each subdivision of the year until the fall of the fourteenth year, when the rates for boys became higher and remained so through the fifteenth year. The maximum growth for girls occurred in the eleventh and twelfth years, and for boys in the fourteenth and fifteenth years. No preadolescent slump in growth was seen.

LEMASTER, Evanston, Ill.

THE SOUTHERN WHITE CLINIC CHILD: A STUDY OF 500 CASES WITH SPECIAL REFERENCE TO DIARRHEA AND OTITIS MEDIA. JOSEPH YAMPOLSKY, South. M. J. **26**:366 (April) 1933.

The author made a study of the relationship between otitis media and intestinal infection in infants. He does not believe that there is any interrelationship.

The children of mothers attending the clinic are being partially weaned at an early age. Cow's milk does not seem to be a substitute feeding. More canned milk is used than cow's milk; this results in diarrhea and underweight.

Severe general weakness and undernourishment are easily responsible for the weakened resistance and are a cause of diarrhea and otitis media in the South.

Ignorance as to feeding results in diarrhea and chronic intestinal indigestion.

The climate is responsible for the aggravation of tonsillitis, otitis media and diarrhea, and these diseases are more typically Southern.

Proper supervision of the milk supply must be made to obtain better results in feeding. This supervision is not carried out in the author's city, Atlanta, Ga.

The importance of prenatal teaching in the South has been stressed too little. As a result, there is much general disorder of digestion in young infants owing to the ignorance of the mothers.

Proper educational facilities should be supplied to the poor so that they may learn the necessity of proper supervision of healthy children.

Syphilis and tuberculosis are on the wane in the South.

Economic conditions are responsible for many of these facts, since pauperism leads to ignorance. However, since many children are weaned by mothers who are not working, the author believes that laziness in the South is also responsible for malnutrition in young children.

SCHLUTZ, Chicago.

THE INFLUENCE OF ACIDOSIS ON CARBOHYDRATE METABOLISM. MARY L. GILCHRIST, Arch. Dis. Childhood **7**:169 (June) 1932.

The effect of a ketogenic diet on the blood sugar curve following the ingestion of dextrose is a rise greater than normal and a delay in the return to the fasting level. During fasting the blood sugar is generally definitely lowered when the subject is on a ketogenic diet.

The ingestion of ammonium chloride occasionally produces a change in the blood sugar curve, but the change is much less marked than that produced by a ketogenic diet.

When the previous diet is ketogenic, the action of insulin is augmented and the effect of epinephrine is diminished.

It is suggested that the alteration in the carbohydrate metabolism caused by a ketogenic diet is due not to acidosis but to a diminution in the stores of carbohydrate produced by this diet.

KELLY, Milwaukee.

MILK PASTEURISATION AS A TECHNICAL PROBLEM. WILLIAM G. SAVAGE, J. Hyg. **33**:42 (Jan.) 1933.

This article is a continuation of studies published in 1931. The difficulties and fallacies of the various methods of pasteurization are emphasized and explained.

Expert opinion strongly favors the low temperature treatment, this temperature being maintained for a given period. Even this method often leaves small areas inadequately heated. Because of the numerous technical problems, some of which are important as indicated by the results, present methods are far from satisfactory.

In determining the efficiency of pasteurization, the author believes that the presence or absence of some bacterial group which is commonly present before treatment (lactose fermenters of Bacillus coli type) and is of about the same heat-resisting ability as Mycobacterium tuberculosis should serve as a guide of efficiency.

JANNEY, Milwaukee.

CELIAC RICKETS. H. J. SEDDON, Proc. Roy. Soc. Med. **26**:153 (Dec.) 1932.

The case reported occurred in a child of 12 years.

WILLIAMSON, New Orleans.

THE RÔLE OF FAT IN PROTEIN METABOLISM. F. MAIGNON, Ann. de physiol. **8**:376, 1932.

In experiments on the white rat, the author found that fat had a higher protein-sparing value than carbohydrate. There was a more favorable nitrogen balance with diets of fat and protein than with diets of carbohydrate and protein. The favorable effect of diets high in fat on diabetic patients who have lost weight and the favorable effect of cod liver oil in any cachectic condition may be due to their effect on nitrogen metabolism.

BUDSON, Ann Arbor, Mich.

PHYSIOLOGY OF CREATININE AND CREATINE. E. F. TERROINE, R. BONNET, P. DANMANVILLE and G. MOURET, Bull. Soc. chim. biol. **14**:12, 1932.

In experiments on pigs it was shown that the ratio of creatinine nitrogen to the total nitrogen of the urine, with the minimum expenditure of nitrogen, is always higher, sometimes considerably so, than the ratio of creatine nitrogen to the total nitrogen of muscle. Fasting causes intense creatinuria, while the loss of nitrogen is increased. It is probable that the creatine thus produced is the result of the degradation of protein.

When intoxication caused by benzoyl hydroxide, phlorhizin or phosphorus is superimposed on a diet permitting a minimum endogenous excretion of nitrogen, there are observed simultaneously an increase in the nitrogen in the urine, a rigorous maintenance of the former rate of excretion of creatinine and an increase in the excretion of creatine. The production of creatinuria by poisons which have as their only common property the increase in the degradation of nitrogen and the parallelism between the excretion of creatine and total nitrogen suggest a formation of creatine, perhaps transitory, in the course of the degradation of certain nuclei of proteins.

With diets quantitatively identical and adequate in every respect, the excretion of creatine by the pig increases as the coefficient of the utilization of nitrogen decreases. The excretion of creatinine is not modified. The metabolism of proteins is accompanied by a more or less abundant formation of creatine, and the higher the value of the protein as a precursor of creatine, the lower is its biologic value.

KUGELMASS, New York.

INSULIN IN THE TREATMENT OF MALNUTRITION IN INFANTS. P. LEREBOULLET and P. BAIZE, Nourrisson **21**:1 (Jan.) 1933.

Cases of simple malnutrition have been markedly benefited, in the authors' experience, by the administration of insulin and dextrose. The favorable reaction is due not only to better carbohydrate metabolism, but also to the improved metabolism of protein and fat and to an avoidance of dehydration. Success is not to be expected in cases of athrepsia or in cases in which an organic disease or a chronic infection is responsible for the debility. A daily dose of 1 unit of insulin per kilogram of body weight is recommended. The treatment is usually limited to three weeks.

MCCLELLAND, Cleveland.

ELIMINATION OF INORGANIC PHOSPHORUS BY THE NORMAL CHILD AND BY THE RACHITIC CHILD FOLLOWING PARENTERAL INTRODUCTION OF ORGANIC PHOSPHORUS. G. CAREDDU and F. RASI, Riv. di clin. pediat. **30**:1517 (Dec.) 1932.

Following the intramuscular injection of 69 mg. of phosphorus in the form of a sodium compound into thirteen rachitic children, the increase in the elimination of inorganic phosphorus in the urine within forty-eight hours was equivalent to an average of 96 per cent (maximum, 119 per cent, and minimum, 70 per cent)

of the phosphorus injected. In ten nonrachitic children the average was a little less than 61 per cent (maximum, 84 per cent, and minimum, 36 per cent). The children with the most active rickets showed the greatest excretion of phosphorus. The system of the rachitic child is apparently quite as capable of changing organic phosphorus to inorganic phosphorus as that of the normal child.

HIGGINS, Boston.

EFFECTS OF REFLECTED ULTRAVIOLET RAYS ON RACHITIC AND SPASMOPHILIC CHILDREN: REACTION OF THE CALCIUM AND PHOSPHORUS OF THE BLOOD; EFFECTS ON GROWTH. P. DANESI, Riv. di clin. pediat. **30**:1581 (Dec.) 1932.

In these observations ultraviolet rays from the mercury vapor arc in quartz were reflected from a white wall to the patient. The maximum time of exposure was fifteen minutes for both the back and the front. Eight infants with tetany and rickets were treated by the reflected rays. Studies of the blood calcium and blood phosphorus showed excellent and rapid cures of tetany and rickets. The author believes that treatment by reflected rays affords a much safer therapeutic procedure than direct irradiation.

HIGGINS, Boston.

WHOLE LACTIC ACID MILK IN THE FEEDING OF YOUNG INFANTS. FRITZ GIERTHMÜHLEN and G. LEMPERT, Kinderärztl. Praxis **3**:450 (Sept.) 1932.

Whole lactic acid milk is the food of choice for premature, atrophic and hypotrophic infants, and for infants with mild cases of pylorospasm. The addition of lactic acid to the usual mixtures of milk seems to render them more antidyspeptic and antirachitic. In the treatment of alimentary disturbances whole lactic acid milk is fully as effective as the other acid foods, e. g., buttermilk and albumin milk.

HUENEKENS, Minneapolis.

HYDROSTASIS. G. BESSAU, Monatschr. f. Kinderh. **57**:162, 1933.

The author reviews the experimental work done by Rosenbaum and himself in which they sought to prove that the syndrome of alimentary intoxication in infants is due to a combination of anhydremia and parenteral infection. He reports a case in which a child with symptoms of alimentary intoxication showed decided improvement in appearance and in the elasticity of the tissues while continuing to lose weight. Although there must have been a loss of water from the body, the tissues themselves were receiving more water.

Bessau reasons from this case that in alimentary intoxication there must be a mechanism causing some hydrostasis or binding of water to prevent it from reaching regions where it is needed. The treatment indicated is to reestablish the circulation of fluids by giving much fluid and cardiac stimulants.

GERSTLEY, Chicago.

BASAL METABOLISM OF CHILDREN IN RESORTS ON THE EAST SEA AND THE NORTH SEA. MAX KLOTZ, Monatschr. f. Kinderh. **57**:239, 1933.

There is a tradition that resorts on the East Sea and on the North Sea have different effects on metabolism. The author subjected groups of children in these localities to metabolic tests. He found that there was little difference between the effect of the localities, but that great differences occurred according to the season of the year and the constitution of the child. Chronically sick and constitutionally abnormal children reacted with an increased metabolism more rapidly than well children. Often a change could be noticed within twenty-four hours. As regards season, the most marked reaction was found during the winter months, and the least marked reaction during summer. Humid, hot weather had a decidedly depressing action. Clinically, it was noted that acute tuberculous processes were influenced unfavorably, while chronic diseases of the lungs and chronic eczema were benefited.

GERSTLEY, Chicago.

COMPOSITION AND DIGESTIBILITY OF BEETS IN ANIMAL FEEDING. ISTVAN WEISER and A. ZAITSCHEK, Zentralbl. f. Tierernahr. **4**:201, 1932.

The composition of sixty beets of six varieties was determined. Digestion trials in vitro of sugar beets used in feeding animals showed 2.62 per cent digestible nitrogen and from 58 to 59 per cent digestible starch (dry basis). The feeding of beets favorably influenced the nitrogen balance, but there was no effect on the calcium or phosphorus balance of the animals fed with beets or with beets plus hay.

KUGELMASS, New York.

RICKETS AND ITS TREATMENT. EMIL WIELAND, Schweiz. Ztschr. f. Hyg. **61**:25 (Jan. 10) 1931.

An interesting historical review of rickets is given, showing its relation to lack of sunshine, i. e., its development in temperate zones when man began to live indoors; its presence on the shady side of a mountain, while children in the same valley on the sunny side are free from it, and its absence in the tropics and the far north where fish (with their "stored sunshine" from eating small fish living on sun-rayed algae and similar food) is an important article of diet. The means for treating rickets are divided into two classes: first, direct light therapy, including ultraviolet radiation from the mercury vapor arc in quartz and direct sunlight, and second, indirect light therapy, including the use of irradiated milks, vegetables, egg yolk and grains, and finally the different preparations of irradiated ergosterol.

LESLIE, Chicago.

Prenatal Conditions

CALCIUM AND INORGANIC PHOSPHORUS CONTENT OF PRENATAL AND POSTPARTUM SERUM. J. W. MULL and A. H. BILL, Am. J. Obst. & Gynec. **23**:807 (June) 1932.

The cord serum (thirty-five cases) contained an average of 11.7 mg. of calcium per hundred cubic centimeters. The average for the mothers (forty-four cases) was 9.8 mg. at the onset of labor, with no significant change at delivery or for two days post partum. On the seventh day post partum the average was 10.4 mg. (forty-one cases); from the twelfth to the fourteenth day, 10.5 mg. (eighteen cases), and after six weeks or more, 10.4 mg. (fifty-two cases, in most of which the infants were nursing). The average normal value (sixty cases) was 10.4 mg. The inorganic phosphorus reached a peak at delivery, averaging 5.1 mg. in thirty-five cases. This was followed by a slight decline and a subsequent recovery to a value slightly higher than the predelivery level. Six weeks post partum, the average was from 3.7 to 3.9 mg. The cord blood averaged 5.8 mg. of inorganic phosphorus in thirty-six cases.

KUGELMASS, New York.

CONGENITAL MALFORMATION OF THE AURICLE ASSOCIATED WITH PARALYSIS OF THE FACIAL NERVE. CLAIN FANNING GELSTON and EMMETT E. SAPPINGTON, Arch. Pediat. **49**:730 (Nov.) 1932.

Gelston and Sappington review the literature on congenital malformation of the auricle associated with paralysis of the facial nerve and report a case. A review of the embryologic development of the external ear is presented in detail, showing how variations in embryologic development result in such deformities.

WADDELL, JR., University, Va.

AMYOPLASIA CONGENITA (MULTIPLE CONGENITAL ARTICULAR RIGIDITY: ARTHROGRYPOSIS MULTIPLEX CONGENITA). WILFRID SHELDON, Arch. Dis. Childhood **7**:117 (June) 1932.

A case of amyoplasia congenita (multiple congenital articular rigidity) is described, and the literature is reviewed. The pathogenesis of the condition is discussed. There is developmental aplasia of certain groups of muscles, followed by secondary developmental defects in the structure of the joints.

KELLY, Milwaukee.

OSTEOPSATHYROSIS (LOBSTEIN'S DISEASE). CONSTANCE M. OTTLEY, Arch. Dis. Childhood **7**:137 (June) 1932.

The characteristic features of Lobstein's disease are (1) fragility of the bones, (2) a peculiar conformation and structure of the bones, (3) a peculiar shape of the skull, (4) laxity of the ligaments, leading to excessive mobility of the joints and in some cases to repeated dislocations, (5) blue coloration of the sclerae, (6) deafness, (7) an abnormal electrical reaction of the muscles, (8) miscellaneous abnormalities, more rarely seen, such as unusually fine hair, white patches in the nails and deficiency of the enamel of the teeth, and (2) the familial character of the disease. Lobstein's disease and osteogenesis imperfecta are compared. Some investigators consider the two conditions unrelated maladies having a superficial resemblance.

KELLY, Milwaukee.

COMPLETE TRANSPOSITION OF THE GREAT VESSELS OF THE HEART WITH A PATENT FORAMEN OVALE. W. M. FELDMAN and A. CHALMERS, Brit. J. Child. Dis. **30**:27 (Jan.-March) 1933.

A boy was admitted to the hospital at 1 month of age; he died at 2 months. He was born at full term. The cyanosis noted at birth became progressively less marked. The area of cardiac dulness was slightly increased, the heart sounds were good, and no murmurs were heard. The skin and mucous membranes were markedly cyanosed. Roentgen examination showed general enlargement of the heart, especially the right side.

The postmortem observations were as follows: The right auricle was greatly enlarged; the pulmonary veins and the superior and inferior venae cavae entered the right auricle. The aorta branched off the right ventricle and lay in front and to the right of the pulmonary artery, which branched off the left ventricle. There was a small opening in the foramen ovale. The left auricle and ventricle were poorly developed.

LANGMANN, New York.

HEREDITARY KNOCK-KNEE, WITH RECURRENT DISLOCATION OF PATELLA AND APLASIA OF NAILS ON FINGERS AND TOES. W. J. RUTHERFORD, Brit. J. Child. Dis. **30**:34 (Jan.-March) 1933.

The author reports a case of congenital knock knee that was caused by a twist inward of a portion of the left tibia. There were five instances of this deformity in three generations, and each affected member showed aplasia of the finger-nails and toe-nails; in some cases there was dislocation of the patella. Stunted growth was also a common finding. Rutherford feels that this complex of conditions cannot possibly be explained in terms of an ectodermal defect alone.

LANGMANN, New York.

ABDOMINAL FETAL IMPLANTATION: RETRO-PERITONEAL TERATOMA. O. L. ADDISON, Proc. Roy. Soc. Med. **25**:1736 (Oct.) 1932.

An infant at birth was observed to have enlargement of the abdomen, and at 9 weeks of age examination revealed a hard, irregular mass which could be palpated in the right side of the abdomen. The results of all investigations are given in the report, as well as notes on the operation and the pathologist's report of tumor.

WILLIAMSON, New Orleans.

DEXTROCARDIA WITH PATENT DUCTUS ARTERIOSUS AND TRANSPOSITION OF VISCERA. A. G. MAITLAND-JONES, Proc. Roy. Soc. Med. **26**:148 (Dec.) 1932.

The author reports a case of dextrocardia in a child of 5 years. The cardiac condition was found during a general examination at the age of 2 years. His general health had been good. He could play without dyspnea, but became very blue whenever he went into a violent temper. His father showed many congenital deformities, and both of his maternal grandparents had suffered from heart disease.

On examination the liver was found on the left, and a barium sulphate meal showed the stomach on the right. The apex beat of the heart was in the fifth space on the right internal to the midclavicular line. An area of cardiac dulness extended to the left sternal border. Systolic murmur and systolic thrill were present. The report is accompanied by an electrocardiogram, an orthodiagram and a teleroentgenogram.

WILLIAMSON, New Orleans.

MEGA-DOLICHOSIGMOID IN AN INFANT. PEARSE WILLIAMS, Proc. Roy. Soc. Med. **26**:152 (Dec.) 1932.

An infant of 11½ months was admitted to the hospital with a greatly distended abdomen in the right half of which was a hard irregular mass. The blood showed "microcytic anemia of chlorotic type." The roentgenogram (opaque meal and enema) showed a very long sigmoid loop which was somewhat enlarged in the transverse diameter. Attacks of colic with tense gaseous and fecal distention occurred at times. Visible peristalsis was occasionally present. Feces were passed, and the infant was for a time in great distress. The tumor was not felt again, as hard feces were not allowed to collect in the loop.

WILLIAMSON, New Orleans.

COARCTATION OF AORTA. WILDRED SHELDON, Proc. Roy. Soc. Med. **26**:154 (Dec.) 1932.

The case reported occurred in a child of 12 years.

WILLIAMSON, New Orleans.

MEDIASTINAL DERMOID AND SPINA BIFIDA. REGINALD LIGHTWOOD, Proc. Roy. Soc. Med. **26**:157 (Dec.) 1932.

An infant of 5 months was admitted to the hospital on account of upper dorsal spina bifida. On examination a round swelling with a depressed center was found in the upper dorsal region. The right side of the thorax was larger than the left. The percussion note was dull over the back and front of the thorax in its upper part, more on the right than on the left. There was no cardiac displacement. Roentgen examination showed an oval tumor occupying the upper part of the mediastinum, but somewhat to the right. The heart was not displaced, and there was no abnormality of the vertebral laminae. The report is accompanied by a roentgenogram.

WILLIAMSON, New Orleans.

CONGENITAL ESOPHAGEAL STENOSIS. STEN ECKERSTRÖM, Acta pædiat. **13**:63 (June 6) 1932.

Esophageal stenosis, which is more rare than atresia, may permit survival but always with limitation of growth and, in certain reported cases, with retardation of sexual maturity.

Eckerström reports the case of a boy, aged 8 years, who had difficulty in swallowing and who at the time of examination was 12 per cent underheight and 44 per cent underweight for his age. Roentgenograms showed a constriction of the esophagus at the about the level of the eighth thoracic vertebra, with great dilatation above it; a fine stream of the opaque meal passed the stricture, but the upper part was not emptied even in half an hour.

With the esophagoscope a diaphragm was seen at the level indicated, showing a small eccentric aperture. This was enlarged with the galvanocautery so as to admit a no. 18 stomach tube, which was left in place for a week. Within the next ten days the opening was dilated to the size of a no. 40 sound. From this time on the patient was able to eat a normal diet without any untoward symptoms. In three months he gained 4.5 Kg. in weight and 2 cm. in height.

MCINTOSH, New York.

CONGENITAL STENOSIS OF THE ESOPHAGUS. LEONARD FINDLAY, Acta pædiat. **13**:70 (June 6) 1932.

In an effort to elucidate the etiology and pathology of congenital esophageal stricture, Findlay has reviewed the eighty cases reported as occurring in children under 15 years of age and has selected for analysis twenty-three of these, in which the nature of the abnormality was demonstrated by autopsy, operation or esophagoscopy. Four types of lesion were identified: (1) narrowing of the lumen (nine cases), (2) membranous diaphragm (four cases), (3) fibrous or fibromuscular thickening of the wall (eight cases) and (4) spasm (two cases). The distribution of these different sorts of obstruction along the course of the esophagus was so varied as to throw doubt on the truth of the familiar clinical aphorism that pathologic narrowings are likely to occur either at the upper or the lower end of the tube or at the level of the bifurcation of the trachea. The same evidence argues against stenosis as being a mild degree of congenital atresia, since the latter always occurs at the bifurcation (from the fourth to the sixth thoracic vertebral body). Simple narrowing and the formation of a membrane represent ontogenetic anomalies. Regarding the origin of the other two types of obstruction, no general statement can at present be made.

McINTOSH, New York.

ECTOPIA CORDIS. C. HEIJL, Acta pædiat. **13**:152 (June 6) 1932.

This article gives a brief description of a case of ectopia cordis associated with anencephaly. The patient lived for sixteen hours. The pericardium was missing, and the heart was covered with skin and a layer of loose areolar tissue rich in blood vessels.

McINTOSH, New York.

SYMPTOMATOLOGY AND DIAGNOSIS OF CONGENITAL DIAPHRAGMATIC HERNIA. N. JOHANNSEN, Acta pædiat. **13**:251 (June 6) 1932.

Diaphragmatic hernia was suspected when an attack of bronchitis at 1 year of age brought on symptoms of intestinal obstruction. Paradoxical movement of an epigastric swelling, which rose on inspiration, was noted, and intestinal gurgling synchronous with the respiratory cycle and occasionally occurring independently could be both heard and palpated over the right anterior portion of the wall of the chest. The diagnosis was confirmed by roentgen examination. The symptoms of intestinal obstruction disappeared spontaneously, and the patient left the hospital clinically well. He was readmitted, however, with acute pneumonia and died at 15 months of age. Autopsy showed a hernial sac attached at the right side of the foramen of Morgagni.

The author reviews the literature on the antemortem diagnosis of diaphragmatic hernia and directs attention to the importance of cyanosis, ileus and particularly the characteristic gurgling sounds. A valuable bibliography is appended.

McINTOSH, New York.

Acute Infections

MALARIA PROPHYLAXIS WITH PLASMOCHIN AND QUININE SALTS. P. F. RUSSELL and R. L. HOLT, Am. J. Trop. Med. **12**:369 (Sept.) 1932.

The authors review briefly the literature on malaria prophylaxis with plasmochin combined with quinine salts and report the results of their investigation concerning the use of this treatment. They conclude that daily doses of 0.01 Gm. of plasmochin and 0.3 Gm. of quinine sulphate, though well tolerated, were not always sufficient to prevent the appearance of malaria parasites in the blood, although occasionally they did. However, they usually forestalled clinical symptoms. Even doses of 0.02 Gm. of plasmochin and 0.6 Gm. of quinine sulphate occasionally permitted a development of parasites in the blood. Further studies are necessary to determine the efficacy of as well as tolerance for larger doses of these drugs.

BURPEE, Augusta, Ga.

METABOLISM AND TREATMENT OF BLACKWATER FEVER. A. MORRIS WAKEMAN, CLARE A. MORRELL, ANNA J. EISENMAN, DOUGLAS L. SPRUNT and JOHN P. PETERS, Am. J. Trop. Med. **12**:407 (Nov.) 1932.

The authors carried out metabolic studies in two cases of blackwater fever in human beings and in five cases of experimental hemoglobinuria in dogs produced by intravenous and intraperitoneal injections of hemolyzed blood. From their studies they conclude that the general similarity of the functional disturbances seen in cases of tropical blackwater fever, hemoglobinuria from other causes and experimental hemoglobinuria produced in dogs by transfusion with their own laked blood indicates that both the clinical symptoms and the pathologic lesions are essentially referable to intravascular hemolysis. Anuria and the lesser grades of renal functional impairment seem to be referable primarily to occlusion of the renal tubules by débris of coagulated blood pigment. Actual cellular injury appears to play a minor part. Vomiting and shock may play an important secondary rôle in the production of anuria or oliguria.

The logical therapeutic procedure would seem to be an early transfusion of blood, when this is not precluded by the appearance of abnormal agglutinins in the blood.

Emesis depletes the stores of salt and water of the body and diminishes the materials required for the production of urine. The rational treatment would seem to be the parenteral administration of saline and dextrose solutions; the oral administration of fluids, because of the vomiting, may only wash out more salt from the body, while the parenteral injections may put an end to the vomiting and restore the fluids of the body to their proper composition.

No support was found for the theory that acidosis occurs in blackwater fever and that the administration of bicarbonate leads to the development of alkalosis.

BURPEE, Augusta, Ga.

INFLUENCE OF RACE IN MALARIAL SPLENOMEGALY IN PANAMA. PAUL S. CORLEY, Am. J. Trop. Med. **12**:467 (Nov.) 1932.

The author examined 1,091 Panama children showing evidence of malaria either by parasites in the peripheral blood or by an enlarged spleen, or by both, to determine the influence of race in malarial splenomegaly in Panama. Five hundred and ninety-eight of the children examined were Negroes, and 493 were Mestizos. Only children of 15 years or younger were used in the survey.

He concluded that splenomegaly as a sign of malaria is more constant in the Mestizo than in the Negro. An enlarged spleen is more likely to be accompanied by parasites in the peripheral blood in a Negro child than in a Mestizo child. In his series one third of the cases of malaria in Negroes and one fourth of those in Mestizos would have been missed had dependence been placed on splenic enlargement alone.

BURPEE, Augusta, Ga.

THE THERAPEUTIC VALUE OF GOLD TRIBROMIDE IN PERTUSSIS. J. EPSTEIN, Arch. Pediat. **50**:38 (Jan.) 1933.

A second communication by this author concerning the value of gold tribromide in the treatment of whooping cough is presented. The disease is discussed from the points of view of morbidity, mortality, anatomic pathology, physiologic pathology, complications and sequelae, diagnosis and treatment.

Epstein has made a study of the various therapeutic procedures employed in the treatment of whooping cough, particularly as regards the bromides, and he feels that gold tribromide is of decided therapeutic value in the treatment of pertussis, the medicinal effect being due to its neurosedative and antibacterial properties. The drug may be given in the form of an elixir, as it is pleasant to take in this form. The dosage varies with the age and the condition of the child and the frequency of the spasms of coughing. As a rule from $\frac{1}{10}$ to $\frac{1}{20}$ grain (0.0065 to 0.003 Gm.) should be given three or four times during the day and at midnight.

WADDELL, JR., University, Va.

THE RELATION OF SMALLPOX MORBIDITY TO VACCINATION LAWS. S. B. WOODWARD and ROY F. FEEMSTER, New England J. Med. **208**:317 (Feb. 9) 1933.

A few months ago an organization opposing vaccination against smallpox distributed broadcast a map of the United States in which the states having laws for compulsory vaccination were colored black; those leaving the decision to local authorities were colored gray; those having no laws for vaccination were white, and those in which laws prohibited compulsory vaccination were marked with a gold star. This map is reproduced, and in each state the total number of cases of smallpox for the ten year period from 1919 to 1928 is indicated. There is also a table showing the total number of cases of smallpox and the incidence per hundred thousand in the different states for the same decade.

Of the states where vaccination is compulsory (black on the map), Massachusetts has the lowest rate, 1, and South Carolina has the highest, 37.4. Of the states with local option (gray), New Jersey has the lowest rate, 3.5, and Oregon the highest, 179.5. Of the states with no compulsory laws (white), Delaware has the lowest rate, 13.6, and Washington the highest, 193. Of the states prohibiting compulsory vaccination (gold star states), Arizona has the lowest rate, 45.1, and Utah the highest, 272. Still more striking is a graph showing that in the ten states where vaccination is compulsory the average rate is 6.6; in the six states with local option, 51.3; in the twenty-nine states with no compulsory laws, 66.7, and in the four gold star states, 115.2.

GENGENBACH, Denver.

DIPHTHERIA IMMUNIZATION AND THE PRIVATE PRACTITIONER. GAYLORD W. ANDERSON and GEORGE H. BIGELOW, New England J. Med. **208**:781 (April 13) 1933.

"There is a quite general feeling among physicians that their personal incomes are impaired by the services offered by health departments. Many are silent about it, feeling that in the long run the public may benefit. Others, particularly during these distressing times, are articulate and refer to the effective health officers as an enemy of the private practitioner."

The Massachusetts Department of Public Health prepares toxin-antitoxin in bottles of 20 cc. for use in the clinic and in ampules of 1 cc. for individual use. Thus the number of ampules used in any community would give some index of the extent of immunization to diphtheria in private practice.

TABLE 1.—*Average Distribution of Toxin-Antitoxin Ampules*

Average Clinic Immunization Rate per Year per 1,000 Population	Average Ampules per Year per 1,000 Population
Less than 5	4.1
5–10	4.8
10–15	6.2
15–20	7.1
20 plus	10.0

If, as the rate of immunization in the clinic increases, that from the use of individual ampules of toxin-antitoxin decreases, the clinic is taking business from the doctor's office; whereas, if they both increase at the same time, the education disseminated by the clinic increases the business of the private doctor.

A group of twenty-six cities and towns with a total population of over 1,600,000 was studied. Table 1 shows the distribution of ampules for the years 1925 to 1931, inclusive, in these communities, grouped according to the intensity of the immunization programs conducted.

In Attleboro and Brookline, a systematic house to house canvass has been made by public health or visiting nurses to urge immunization on the parents. That they should have shown the highest level of private immunization of any communities studied seems more than mere chance. Attleboro showed a rate

of immunization for the clinic of 22.8 per thousand population and for private practice, 22.6; Brookline showed a rate of 10.6 and 26.1, respectively. Brookline, however, is a rather affluent community.

1. It appears that in the 1,600,000 population in twenty-six communities studied, those showing the highest rate of public immunization against diphtheria show also the highest rate of private immunization.

2. Those communities in which the most public (and therefore private) immunizations are done show the greatest improvement in incidence of diphtheria over seven years.

GENGENBACH, Denver.

CURRENT PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES. Pub. Health Rep. **48**:163 (Feb. 17) 1933.

The incidence of influenza during the period from Jan. 1 to Jan. 28, 1933, was several times higher than that for the corresponding period of the preceding three years. Reported cases of meningococcus meningitis showed an increase of about 50 per cent over those of the same four week period of the previous year, especially in the north and south central states. Owing to an outbreak of typhoid fever in Chamberlain, S. D., the incidence of this disease in the country as a whole showed an increase instead of the usual seasonal decrease. Diphtheria, poliomyelitis and smallpox showed an appreciable decrease as compared to the incidence of these diseases during the first four weeks of January in recent years. The incidence of scarlet fever was slightly higher than usual, but measles was less prevalent than during this period of the last two years.

LEMASTER, Evanston, Ill.

CHRONIC ENTERIC CARRIERS AND THEIR TREATMENT. C. H. BROWNING, H. L. COULTHARD, R. CRUICKSHANK, K. J. GUTHRIE and R. P. SMITH, Medical Research Council, Special Report Series, no. 179, London, His Majesty's Stationery Office, 1933.

This study of chronic carriers of the typhoid-paratyphoid group furnishes a definite contribution to the present knowledge of this subject. Eight intestinal excreters, two urinary carriers and four patients with postenteric perichondritis or osteomyelitis were investigated thoroughly. The identification of carriers depends on the isolation of the specific organism from discharges and secretions. The most effective methods for the detection of carriers are discussed. Subsidiary tests such as the Widal test, the opsonic index and the sensitivity of the skin are of value if positive, but in general they do not give valuable information, since carriers not infrequently give negative reactions. In the treatment of chronic enteric carriers the results were ineffective with nonsurgical measures, such as drug therapy, diet, physical therapy and vaccines. In cases in which the gallbladder was the site of infection, surgical measures directed toward it yielded highly satisfactory results. It is thought that carriers constitute the chief means of spread of typhoid and paratyphoid fever; consequently their detection and treatment are of paramount importance in eradicating these diseases. The literature on this subject is reviewed.

LEMASTER, Evanston, Ill.

TREATMENT OF SCARLET FEVER. M. DE BIEHLER, Arch. de méd. d. enf. **36**:95 (Feb.) 1933.

The author was among the first to use the vaccine of Gabryczewski, developed in 1914, in the prevention of scarlatina, and he has been an enthusiastic advocate of antiscarlatinal serum in all but the mildest cases since the publication of the epochal contributions of the Dicks and of Dochez.

In 127 cases of varying gravity in which the patients were treated by this method de Biehler reports but one death. Excellent results were also obtained in the prevention of serum sickness through the regular administration of calcium in the form either of the lactate or of the chloride, in doses of 6 Gm., well diluted, three times a day. The author recommends universal active immunization of children.

AMESSE, Denver.

TREATMENT OF DIPHTHERITIC PARALYSIS. JULES RENAULT and PIERRE-PAUL LÉVY, Bull. Soc. de pédiat. de Paris **30**:214 (April 19) 1932.

Antidiphtheritic serum had no demonstrable effect in a number of cases of postdiphtheritic paralysis. In an effort to release the toxin which was bound to the tissues, the authors used a mixture of toxin which was hyperneutralized with antitoxin. This gave slight reactions but produced no rapidly curative results.

BENJAMIN, Montreal, Canada.

HEMIPLEGIA AND APHASIA FOLLOWING MEASLES. BABONNEIX, RIOM and WILM, Bull. Soc. de pédiat. de Paris **30**:222 (April 19) 1932.

A girl, aged 2 years, had a severe attack of measles. On the eighth day of the illness, after the acute symptoms had subsided, she suddenly became cyanosed while drinking a cup of milk and fell. She held the right arm stiff against the body, after it had undergone a few clonic contractions, and fell into a deep sleep. There were repeated muscular contractions on the right side of the body during the sleep. The following day there were facial paralysis on the right side and paralysis of the right arm and the right leg, and she could not speak. The case is considered one of encephalitis following measles.

BENJAMIN, Montreal, Canada.

STUDIES OF GLYCEMIA IN SCARLET FEVER, MEASLES AND CHICKENPOX. L. MANZONI, Riv. di clin. pediat. **30**:1559 (Dec.) 1932.

The author found a tendency for the blood sugar content to be higher in the febrile stages of scarlet fever and measles than when the temperature of the body had become normal; in no case was glycosuria present. In patients with chickenpox the blood sugar content did not vary from the findings in normal healthy persons.

HIGGINS, Boston.

BLEEDING IN THE COURSE OF DIPHTHERIA. PAUL KISS, Arch. f. Kinderh. **98**:193 (Feb. 21) 1933.

Of 1,680 patients with diphtheria treated at the University Children's Clinic in Budapest between 1920 and 1931, there were 86 in whom bleeding of some kind occurred. The mortality was only 2.6 per cent for the patients showing nasal bleeding associated with nasal diphtheria. When bleeding from the nose occurred in patients in whom the diphtheritic membrane was confined to the tonsils or the conjunctivae, the mortality was 11.1 per cent. A mortality of 44.5 per cent was seen in cases of nasal bleeding in which there were diphtheritic membranes in both the nose and the throat. The prognosis was extremely bad when bleeding from more than one source occurred.

LEMASTER, Evanston, Ill.

EFFECT OF SERUM ON THE APPEARANCE OF THE COMPLICATIONS OF SCARLET FEVER. MARIA HAUF, Arch. f. Kinderh. **98**:244 (Feb. 21) 1933.

In a series of 248 cases of scarlet fever, every alternate patient was given scarlet fever streptococcus serum (Bering-Werke, Marburg). Those receiving serum showed a slightly higher incidence of complications and also a greater number of severe and moderately severe cases than the control group. In spite of these results, the author believes that the serum is of value in combating the toxic condition occurring during the first few days of the disease.

LEMASTER, Evanston, Ill.

OCCURRENCE OF TOXIN-PRODUCING STRAINS OF HEMOLYTIC STREPTOCOCCI IN PERSONS EXPOSED TO SCARLET FEVER. N. LÖNBERG, Acta pædiat. **13**:340 (June 6) 1932.

In a military unit of 427 men an outbreak of 6 cases of scarlet fever occurred within two weeks. Dick tests were performed on the entire unit, and 114 gave positive reactions. Cultures were made from the throats of these men and from

those of the staff of the infirmary and the kitchen, a total of 133 men; of these, 27 showed hemolytic streptococci. Twenty-five of the strains were tested for toxin-producing power; 15 produced abundant toxin, and the rest, detectable but feebler amounts. None of the subjects harboring the streptococci—even the most potent toxin-producing strains—and giving positive reactions to the Dick test contracted clinical scarlet fever.

McINTOSH, New York.

STREPTOCOCCUS SEPTICEMIA IN CHILDHOOD. P. NOBÉCOURT, Acta pædiat. **13**:374 (June 6) 1932.

The author limits his discussion to bacteriemias which begin suddenly and which cannot be shown to be secondary to an infected wound. The portal of entry is usually the upper respiratory tract. Symptoms are generally ushered in with a chill and severe pyrexia. Acute and fulminating types may be distinguished. The outlook is grave, and treatment is unsatisfactory.

McINTOSH, New York.

Chronic Infections

A SURVEY OF ONE HUNDRED CASES OF CONGENITAL SYPHILIS TREATED WITH STOVARSOL (ACETARSONE). HAROLD A. ROSENBAUM, J. Pediat. **3**:434 (Sept.) 1933.

This is a clinical report of the results obtained from treating a hundred congenitally syphilitic children by means of acetarsone. There were only five toxic reactions. Serologic reversal was much more frequent after one or two courses than with older methods of treatment. The dosage recommended by Bratusch-Marrain was followed. Improvement in symptoms and in the physical findings occurred rapidly after the treatment was begun.

LEMASTER, Evanston, Ill.

TUBERCULOSIS IN INFANCY AND CHILDHOOD: A STATISTICAL STUDY. MIRIAM G. KATZEFF, New England J. Med. **209**:83 (July 13) 1933.

This study includes the total number of patients admitted annually to the Children's Hospital of Boston with a condition diagnosed as tuberculosis, from 1884 to 1931, and a comparative statistical study of the orthopedic and nonorthopedic forms.

Admissions to the hospital have increased from 914 cases in 1884 to 15,789 cases in 1930. The highest incidence of tuberculosis occurred in 1884 and 1885 (9 per cent and 10 per cent, respectively). The lowest figure was in 1927 (1 per cent). The percentage of orthopedic forms from 1884 to 1903 varied from the highest in 1886 (100 per cent) to the lowest in 1897 (70 per cent). During this period the nonorthopedic forms of tuberculosis were few in number, no more than 19 per cent, which occurred during 1888.

Probably the most interesting story told by the statistical study occurs from 1924 to 1930. During this period both the number and the percentage of orthopedic forms show a steady decline, reaching the lowest point in 1930 (22 per cent), while during these years the nonorthopedic forms steadily increased to reach a percentage of 77.7 in 1930. This reversal of position of orthopedic and nonorthopedic forms of tuberculosis since 1924 leads to the thought that the practice of preventive medicine is more successful in combating the orthopedic forms of tuberculosis.

GENGENBACH, Denver.

ON PREVENTIVE VACCINATION AGAINST TUBERCULOSIS WITH BCG AS PRACTICED BY DOCTORS IN THEIR FAMILIES. A. CALMETTE, Brit. J. Tuberc. **27**:1 (Jan.) 1933.

BCG was first used for the prevention of human tuberculosis in 1924, and its use has become so widespread in France that in 1932, 1 in every 5 new-born infants was vaccinated. During that year requests were made of 282 doctors who

were known to have vaccinated their own children for information regarding their observations of these children and their opinion as to the value of B C G. Exactly 280 responses were received. The total number of children vaccinated was 514. The number under 1 year of age was 91, and the number from 1 to 9 years of age, 423. Of these children, 60 had lived in contact with tubercle bacilli, and 43 had probably been definitely exposed to infection. One hundred and forty had been revaccinated once or twice. Seven children had died, in only 1 of whom was there a presumption of tuberculosis. The health of this vaccinated group as a whole was reported as good, only 4 children being designated as but "passably well or sickly." Without exception, these 280 doctors agreed that the vaccination is harmless. The majority of those reporting declared that every viable new-born infant should be vaccinated regardless of environment. Calmette, however, does not advocate compulsory vaccination, holding that it would be a psychologic error to impose it by law before it had become an established prophylactic habit.

The conclusions from this inquiry confirm those furnished by 46 reports from foreign scientists, which may be summarized as follows: 1. Vaccination with B C G is perfectly harmless. 2. Preventive vaccination with B C G practiced on a large scale causes important diminution of general infantile mortality. 3. Children vaccinated with B C G resist children's diseases better than do non-vaccinated children. 4. There will be no return to virulence on the part of B C G in the organism of vaccinated children. 5. Revaccinations by mouth should be practiced at 1, 3, 7 and 15 years of age.

EUGENE SMITH, Ogden, Utah.

THE QUANTITATIVE WASSERMANN REACTION AS A GUIDE TO THE TREATMENT OF SYPHILIS: A PRELIMINARY COMMUNICATION. J. LOVE and H. M. BUTLER, M. J. Australia **1**:727 (June 17) 1933.

The authors recommend the routine use of the quantitative Wassermann test in which the test is performed with the patient's serum in dilutions of 1:40, 1:80 and 1:160, in addition to the usual dilutions of 1:5, 1:10 and 1:20. When fixation is not complete in any tube, the proportion of unlysed cells (determined by comparison with the controls) may be used to estimate the dilution at which complete fixation would have occurred. If the tests are performed at regular monthly intervals and the results are plotted on a chart similar to a Vernes chart, along with the type of treatment and other pertinent facts, a definite index to the progress of the patient and a plain guide in regard to treatment are available.

GONCE, Madison, Wis.

RECURRING COLLAPSE OF LUNG WITH ENLARGED MEDIASTINAL GLANDS? EPI-TUBERCULOSIS. T. PEARSE WILLIAMS, Proc. Roy. Soc. Med. **26**:1008 (June) 1933.

An infant 42 weeks old was noticed to become cyanosed when enraged. Over the mesial half of the upper and middle lobes of the right lung anteriorly and the apex of the lower lobe posteriorly the percussion note was impaired, and diminished entry of air with a few scattered râles was present. A roentgenogram was taken, and the roentgenologist suggested an epituberculous collapse due to glandular enlargement. Three weeks later the temperature rose to 103 F., and signs of consolidation appeared. A week later the temperature became normal and remained so, and the roentgenogram showed a great improvement of the lung over the condition shown in the previous picture. Two months later the signs returned, and a third roentgenogram showed much the same condition as the first.

WILLIAMSON, New Orleans.

CONGENITAL NEUROSYPHILIS. L. BABONNEIX and M. FAYOT, Arch. de méd. d. enf. **36**: 200 (April) 1933.

Continuing their pioneer work on hereditary syphilis of the nervous system, the authors report a series of sixty-three cases which they classify into groups representing spasmoparalytic, epileptic and choreic phenomena respectively.

The first variety is still further divided into unilateral and bilateral invasions. Psychic manifestations of this grave affliction of childhood are also discussed in detail, from the gross types of idiocy to conditions affecting the emotions and the character. Mixed types having a syndrome involving both the motor and the intellectual functions are illustrated with clinical histories.

The conclusion is drawn that inherited syphilis is responsible for many of the infantile encephalopathies, others having their origin, as Comby and others have demonstrated, in neurotropic viruses or in acute eruptive fevers.

AMESSE, Denver.

SPONTANEOUS PNEUMOTHORAX IN A TUBERCULOUS INFANT. B. LOZADA ECHENIQUE and J. M. PAEZ DE LA TORRE, Arch. de méd. d. enf. **36**:295 (May) 1933.

Cases of spontaneous pneumothorax in subjects under 1 year of age are extremely rare; no other instance, for example, has been reported from the Argentine Republic. The authors publish in detail, with numerous illustrations, the history of an infant of 10 months whose mother suffered from tuberculosis. Examination on admission showed tuberculous bronchopneumonia with cavitation and pneumothorax of the right lung, confirmed by autopsy several months later.

AMESSE, Denver.

PREVENTION OF CONGENITAL SYPHILIS. E. LESNE and LINOSSIER-ARDOIN, Nourrisson **21**:38 (Jan.) 1933.

The most important single factor in the prophylaxis of congenital syphilis is adequate antisyphilitic treatment of the mother during or before the pregnancy. Routine serologic tests are advised for the detection of latent syphilis. In this way the incidence of congenital syphilis has been reduced from 85 to 19 per cent. Infants born of syphilitic mothers should be under treatment or observation for a period of five years. It is important that the antisyphilitic therapy during pregnancy be thorough.

MCCLELLAND, Cleveland.

TUBERCULOUS PERITONITIS IN INFANCY. L. WILLEMIN-CLOG and F. ARTS, Rev. franç. de pédiat. **8**:599, 1932.

Three forms of tuberculous peritonitis exist: (1) the ascitic form, the least common, which has an insidious onset in vomiting and alternate diarrhea and constipation, with progressive enlargement of the abdomen; (2) the fibrocaseous form, the most frequent, characterized by practically no definite symptoms except enlargement of the abdomen (examination reveals irregular tumor masses), and (3) the tympanic form, characterized by anorexia and enlargement of the abdomen. The temperature is either normal or subnormal, and the extremities are wasted. The treatment is essentially medical; laparotomy has been abandoned. Sun baths and ultraviolet irradiation are the chief therapeutic aids. The tympanic form is always fatal. The other types may be cured.

SANFORD, Chicago.

MEDIASTINOPULMONARY ACTINOMYCOSIS IN A BOY OF SIX YEARS. A. BOLLETTINO, Riv. di clin. pediat. **31**:308 (March) 1933.

The author reports the case of a boy of 6 years with actinomycosis involving not only the glands of the neck and the axilla, but those of the mediastinum and the lungs. The diagnosis was made by culture from a discharging gland and by roentgen examination. The treatment was by iodides, by surgical removal of fistulas and by roentgen irradiation.

HIGGINS, Boston.

PURULENT CONJUNCTIVITIS IN CONGENITALLY SYPHILITIC NEW-BORN INFANTS. PEDRO CANTONNET and HECTOR CANTONNET, Arch. de pediat. d. Uruguay **4**:81 (March) 1933.

Purulent conjunctivitis has an unfavorable prognosis in congenitally syphilitic new-born infants. The low vitality and low resistance of these infants are probably factors. The authors advise early prophylaxis.

SCHLUTZ, Chicago.

MODERN CONCEPT OF INFANTILE PULMONARY TUBERCULOSIS. G. FORTEZA MARTI, Méd. latina **6**:124 (March) 1933.

When the Koch bacillus is implanted in pulmonary tissue its secretion sets up a special process of chemotaxis which causes it to become surrounded by lymphocytes and polymorphonuclear leukocytes. By means of their lipolytic ferment the lymphocytes destroy the mucilaginous casing of the bacillus, and in this state the body is attacked by the proteolytic ferment of the polymorphonuclear leukocytes. If the bacillus is completely destroyed, the condition is that of a cured small initial lesion. But if the organism is not destroyed, it sets up a desquamative lesion surrounded by epithelial cells, including a number of epithelioid forms; that is, a typical lesion begins to form. In fact, the tuberculous toxin surrounding the cells diminishes their reproductive capacity, with the result that their nuclei divide but not the cell bodies, which seem to enlarge, forming giant cells. The effect of the toxin in other areas at a distance is not so intense, but is decided enough to weaken their activity in the production of intercellular substance and to impair their ability to organize connective tissue. Thus there is formed a zone of embryonal cells constituting an imprisoning barrier, which serves as a central lesion without circulatory irrigation, and in this way the degenerative process of caseation is instituted. But if anywhere during this state of affairs the defensive forces of the organism prevail, the cells of the invading embryonal zone will recover their property of forming intercellular fibrous tissue, connective and reparative. In this way a process of fibrosis develops. Following the gradual and regular deposition of calcareous salts there takes place a process first of fibrocalcinosis and later of definite calcification, an occurrence which indicates the complete cure of pulmonary tuberculosis in children and adults.

VINTON, Richards, Mo.

CARDIOVASCULAR SYPHILIS WITH HEMIPLEGIA IN A THREE YEAR OLD CHILD. VLADIMIR MIKULOWSKY, Monatschr. f. Kinderh. **58**:306, 1933.

The author reports the case of a 3 year old child in whom complete right-sided spastic hemiplegia with aphasia suddenly developed. The condition was ascribed to cardiovascular syphilis.

GERSTLEY, Chicago.

TUBERCULOSIS IN CHILDHOOD. S. A. SIWE, Acta pædiat. **14**:274 (April 28) 1933.

In this study, made in the pediatric clinic of the University of Lund, 2,426 patients free from signs of clinical tuberculosis were given the tuberculin test over a period of eleven years. Up to the age of 1½ years the Pirquet test was used, and above this age, the Mantoux test, with 0.01 and 1 mg. of tuberculin, until a positive or a definitely negative result was obtained. No test was considered positive unless redness and infiltration lasted at least forty-eight hours and had been observed to increase during the latter part of this interval. In a small number of cases a definitely positive test was not observed until from the third to the sixth day after injection.

The tables and curves of age distribution of positive tuberculin tests agree closely with some of those recently reported from American clinics; in the third year there are 18.1 per cent of positive tests; in the seventh year, 34 per cent, and in the thirteenth year, 64 per cent.

The procedures used have enabled the author to make a satisfactory comparison of the various tuberculin tests commonly employed. A negative Mantoux test with 1 mg. of tuberculin is almost certain proof (over 98 per cent) that tuberculosis is not present. Depression of allergy in the course of acute infections is neither as marked nor as long lasting as is commonly supposed. Good evidence is brought forward to show that the sensitiveness to a small dose (0.01 mg.) of tuberculin in tuberculous patients is greatest during the first year of life and diminishes progressively up to the ninth year.

McINTOSH, New York.

CERTAIN CLINICAL CONSIDERATION OF IMMUNITY AND ALLERGY IN TUBERCULOSIS. ARVID WALLGREN, Acta pædiat. **14**:544 (July 12) 1933.

Wallgren defines immunity in tuberculosis as an increased resistance toward exogenous reinfection. Allergy he regards as that modification in manner of reacting to a pathogenic agent which a person acquires by virtue of having reacted to the same agent antecedently. Although he does not consider allergy and immunity identical, he does regard them as simultaneous. He summarizes his remarks in the following sentences:

1. Children who have been infected by the tubercle bacillus become sensitive to tuberculin at the time of the appearance of allergy.
2. Children who are sensitive to tuberculin have an increased resistance to exogenous reinfection.
3. There exists no proof that persons who do not react to tuberculin possess any augmentation in their specific resistance to tuberculous infection. (Hence, children whose reaction to tuberculin is not rendered positive by vaccination with B C G should not be considered to have been successfully immunized, as certain authors have insisted.)
4. There is no parallelism between the degree of cutaneous sensitivity to tuberculin and the degree of constitutional hypersensitivity or specific immunity.

McCUNE, New York.

THE MICROSEDIMENTATION TEST IN PULMONARY TUBERCULOSIS IN CHILDREN. AXEL FRIEDLAENDER, Acta pædiat. **14**:550 (July 12) 1933.

Having observed the profitable use of the Langer-Schmidt microsedimentation test in Kleinschmidt's clinic in Hamburg, the author adopted it in the children's hospital Fuglebakken, in Copenhagen. Short sedimentation tubes are used (diameter, 2.5 mm.; height of blood column, 25 mm.); the scale on the tubes is divided in millimeters. A 5 per cent solution of sodium citrate is aspirated to a certain mark; 0.12 cc. of blood is drawn up; mixing is accomplished in a porcelain dish, and the mixture is drawn up to the mark 0. The lower end is closed by standing the tube in mercury. The result is read after one hour. The normal values fall between 0 and 10 mm. Values of from 12 to 15 mm. are designated as "high," and those from 15 to 25 mm. as "very high." The values obtained by this method are not directly comparable with those obtained with the macromethods, but there is a definite proportionality between the two methods. The studies of Hocker show that in persons with normal sedimentation rates there is 86 per cent agreement between the Langer-Schmidt and the Westergren methods. In cases of moderate increase in rate (microvalues between 12 and 15 mm.) the macrovalues are 1.9 times as great as the corresponding microvalues. In cases with marked increase in the sedimentation rate, multiplication of the microvalues from 15 to 25 mm. by 2.76 gives the corresponding macrovalues.

The material of this study comprises a hundred children between the ages of 2 months and 12 years with a positive tuberculin reaction. Sedimentation tests were done at regular intervals. The shortest period of observation was one month, and the longest, nine months.

Sixty-seven of the patients had active pulmonary tuberculosis. In forty-three of these patients the microsedimentation test gave high values at some time during

the period of observation, although this elevation was not constant. A rise in the microsedimentation rate was associated with some demonstrable aggravation of the general condition of the patient. The sedimentation rate was accelerated by the onset of exudative pleurisy, erythema nodosum and abdominal tuberculosis with ascites and by the rapid progress of pulmonary tuberculosis.

The worth of the test is depreciated by the fact that the values were normal in seventeen of forty-eight patients in whose gastric contents tubercle bacilli were found and also by the fact that twenty-four of the sixty-seven patients with active pulmonary tuberculosis had consistently normal sedimentation rates. Strikingly low values were also found in miliary tuberculosis, especially when there was associated tuberculous meningitis.

The author concludes that a consistently high microsedimentation value is suggestive of an active tuberculous process, and that a distinct rise in the rate calls for caution in the estimation of prognosis. A consistently normal rate supports the assumption of a latent process unless other findings indicate the contrary. The practical applicability of the test is limited largely to those cases in which it may lend additional evidence to the clinical diagnosis of latent tuberculosis.

McCune, New York.

Erythema Nodosum and Later Tuberculosis. H. J. Ustvedt and A. S. Johannessen, Norsk mag. f. lægevidensk. **94**:532 (May) 1933.

Three hundred and twelve persons were followed for years after an attack of erythema nodosum; the longest period of observation was seventeen years. Clinical tuberculosis occurred in 10 per cent of these patients during the first year after discharge from the hospital. In the succeeding four years tuberculosis was found in only 1 per cent, and after the fifth year following the attack no clinical tuberculosis was detected.

The authors believe that this finding may be interpreted as an indication that erythema nodosum is a phenomenon of hypersensitivity to the tubercle bacillus.

Toverud, Oslo, Norway.

Internal Diseases

Gaucher's Disease: Report of 2 Cases, with a Remission in 1 Following Administration of Liver Extract. Eugene B. Potter and Colin C. McRae, Am. J. M. Sc. **185**:92 (Jan.) 1933.

A brief but comprehensive report of two additional cases of Gaucher's disease, bringing the total number of reported cases to over one hundred, is presented. Photographs showing the characteristic Gaucher's cells accompany the article. The case reports are on a girl (Negress) of 12 years and a white youth of 17 years. The Negress improved promptly following splenectomy, and the youth, who was given liver extract without splenectomy, improved both symptomatically and physically, looking and feeling better than he had for years. Transfusions were of no avail. Although lacking any knowledge of the modus operandi, the authors suggest liver extract in the treatment of Gaucher's disease. It is felt that since this substance was of proved value in the treatment of primary anemias as well as in some other varieties, it may prove helpful in Gaucher's disease.

Henske, Omaha.

Oysters and Anemia. E. J. Coulson, Harold Levine and Roe Remington, Am. J. Pub. Health **22**:1141 (Nov.) 1932.

Realizing the frequency of nutritional anemia prevalent in children between the ages of 3 months and 2½ years, the authors studied the value of oysters, which are known to be rich in the inorganic elements iron, copper and maganese. Oysters from the mid-Atlantic coast contain a relatively greater quantity of these elements than those from the north or south. Analyses of various foods are given,

showing that no other commonly used food except liver surpasses the oyster in amounts of iron and copper in the average serving.

In the study, rats were made anemic and then each was fed an equivalent of 0.5 Gm. of oysters a day. This yielded from 0.137 to 0.523 mg. of iron a day, depending on the source of the oysters. During eight weeks 16.06 mg. of hemoglobin was developed. A control group received milk and iron. This did not give comparable results.

PARKER, Rochester, N. Y.

PATHOLOGIC CHANGES IN THE EAR IN NIEMANN-PICK'S DISEASE. JOSEPH G. DRUSS, Arch. Otolaryng. **15**:592 (April) 1932.

Niemann-Pick's disease starts usually at about the age of 5 or 6 months. There are retarded mental and physical development, enlargement of the abdomen because of the enlarged liver and spleen, and brownish discolorations of the skin. There are low grade fever, anemia and cachexia, and the child usually dies of some intercurrent infection before the age of 2 years. The condition is occasionally associated with amaurotic idiocy. Pathologically there is a general disturbance of the lipoid storage of congenital origin, and many of the organs reveal large round or polygonal cells with pale cytoplasm containing many variably sized and shaped vacuoles; hence the name "foam cells." The vacuoles are thought to be lecithin and are demonstrated only by a special stain. Other fat-chemical changes are present. The foam cells originate from the reticulo-endothelial system and are found in most of the soft tissues.

Embryonic tissue persists a long time in the ear. This fact caused the author to make a special study of the ear in a case of Niemann-Pick's disease, and his report lays special stress on this structure. Most of the tissues of the ear contained foam cells.

BARNETT, Chicago.

SPLENECTOMY IN THE TREATMENT OF HEMORRHAGIC PURPURA. JOHN MARTIN ASKEY and CLARENCE G. TOLAND, Arch. Surg. **26**:103 (Jan.) 1933.

A typical case of chronic hemorrhagic purpura is reported in which splenectomy was performed twenty-two years after the first evidence of the disease. The end-result of the operation as seen a year later was a clinical cure, but there was only moderate hematologic improvement. The literature is also reviewed in order to show in which types of cases splenectomy is of greatest value.

KAISER, Rochester, N. Y.

HIGH CARBOHYDRATE LOW FAT DIET FOR DIABETIC CHILDREN. HEBER C. JAMIESON, Canad. M. A. J. **27**:389 (Oct.) 1932.

The author reviews a series of cases in which the patients had been put on a diet high in carbohydrates and low in fats. The standard diet on admission for children is composed of 100 Gm. of carbohydrates, 60 Gm. of protein and 40 Gm. of fat. If sugar disappears on this regimen, carbohydrate is added at the rate of approximately 25 Gm. daily, with an increase of the protein, which is unavoidable considering the suitability of the food. Insulin is frequently given on admission to hurry the increase of tolerance for dextrose. It is gradually diminished as tolerance is established.

The author's conclusions are as follows:

1. Children are more energetic on this diet than on previous diets high in fat with a similar caloric value.
2. Children relish the food more and give better cooperation.
3. All substitutes for bread and fillers may be dispensed with.
4. This diet increases the tolerance for dextrose in many cases, and in some cases the amount tolerated is double what it was before.
5. Sugar in the urine in persons on this diet is usually increased at first, but it gradually diminishes.
6. Cholesterol falls quickly, but it may rise again to even greater heights than with diets high in fat.

MOORE, Omaha.

PRIMARY CARCINOMA OF THE LIVER IN INFANTS AND YOUNG CHILDREN. GEORGE R. PIRIE, Canad. M. A. J. **27**:401 (Oct.) 1932.

This is a report of three cases, in which the patients were admitted to the Hospital for Sick Children, Toronto.

There have been reported in the literature forty-four cases of primary carcinoma in children. These three bring the total up to forty-seven cases.

In children under 1 year of age, there have been reported fourteen cases; from 1 to 5 years, nine cases; from 6 to 10 years, eight cases; from 10 to 16 years, fourteen cases; age not specified, two cases. There were twenty-one males and seventeen females; in nine cases the sex was not specified.

The first case reported by the author was in a boy, 8 months of age. The baby died within twenty-four hours after admission. The chief complaints on admission to this hospital were intermittent diarrhea and periods of vomiting, projectile in type and occurring about every forty-eight hours. The total gain in weight during the eight months was 8 pounds (3,628.74 Gm.). Autopsy showed a primary carcinoma of the liver.

In case 2, a boy, aged 8 months, was presented for examination because of the size of the abdomen, which had been increasing since birth. There was frequent projectile vomiting. Autopsy showed primary carcinoma of the liver.

In case 3, that of a girl, aged 11 years, an operation for appendicitis was performed. A small mass attached to the bowel in the right quadrant, well up under the liver, was noted. The growth increased in size following the first laparotomy, and the child came in for removal of the tumor six months later. Pathologic examination of the tumor showed carcinoma of the liver.

This patient was still living and apparently normal at the time of the report.

MOORE, Omaha.

EXOPHTHALMIC GOITER IN CHILDREN. LINDON SEED and HENRY G. PONCHER, Illinois M. J. **43**:61 (Jan.) 1933.

Exophthalmic goiter is a rare disease in children below the usual age limit of 12 years. The peak of incidence occurs about the age of puberty, at which time functional changes occurring at that period may be mistaken for exophthalmic goiter. The differential diagnosis is discussed under six headings: (1) persistent tachycardia, with elevated blood pressure and pulse pressure; (2) nervousness and tremor; (3) enlargement of the thyroid; (4) exophthalmos; (5) loss of weight and strength in the presence of a good appetite, and (6) an increased basal metabolic rate. An attempt is made to evaluate their diagnostic importance. Diagnosis is stressed because it is obvious that it is the most important prerequisite in successful treatment.

BARBOUR, Peoria, Ill.

BACTERIOLOGICAL STUDY OF ACUTE ENTERITIS IN INFANTS AND YOUNG CHILDREN. M. L. COOPER, J. Bact. **25**:90 (Jan.) 1933.

Forty-six patients, most of whom were infants, were studied; the mortality rate was 34.7 per cent. Five were studied at necropsy, and from the involved small intestine of each a green-producing streptococcus was isolated; this same streptococcus was shown to be present in the intestinal tracts of 65 per cent of these patients. Seventy-four per cent of these patients had a preceding infection of the upper respiratory tract, and this streptococcus was found present in the intestinal tracts of 65 per cent of this group.

Ninety rabbits were inoculated intravenously with this micro-organism; 70 per cent died, and 92.4 per cent showed marked gross pathologic changes in the small intestine. Streptococci were recovered from the small intestine in 80 per cent of the cases in which cultures were made; thirty-seven rabbits were inoculated with the recovered streptococci; 70 per cent of them showed the same gross pathologic changes, and from these the same streptococci were re-isolated.

Six monkeys were inoculated with this streptococcus, and all became sick; the micro-organism was isolated from the stools of all six after injection while it

had not been present before injection. In five diarrhea developed. Five died. Five showed marked gross and microscopic pathologic changes in the small intestine, and the same streptococcus was isolated from the involved intestinal tracts of all of them; these streptococci when reinjected into other animals produced a similar pathologic picture.

This streptococcus was also isolated from the blood in a fatal case and produced the same pathologic changes in the intestinal tracts of a series of seventeen rabbits, three monkeys and several mice. A similar streptococcus isolated from the throat of one of these patients with an acute infection of the upper respiratory tract produced the same lesions in the intestinal tracts of inoculated animals. It was possible to protect the experimental animals with specific immune serum.

The microscopic pathologic changes in the involved intestinal tracts were as follows: extreme congestion of the mucosa; hemorrhages into the lymphoid nodules; the presence of polymorphonuclears and monocytes in the mucosa and of gram-positive diplococci in the mucosa and submucosa. STOESSER, Minneapolis.

THE COPPER AND NON-HEMOGLOBINOUS IRON CONTENTS OF THE BLOOD SERUM IN DISEASE. ARTHUR LOCKE, E. R. MAIN and D. O. ROSBASH, J. Clin. Investigation **11**:527 (May) 1932.

A method is given for the determination of iron and copper extractable from serum by trichloracetic acid. A study was made of the copper and iron levels in the blood serum of one hundred normal and diseased persons and of thirty-two animals used in control experiments performed to determine certain factors which affect the levels observed in the human subjects.

In normal persons who have fasted for twelve hours the average value for iron in the serum was 1 microgram per cubic centimeter in young men and 0.77 microgram per cubic centimeter in young women. After longer periods of fasting these values were higher. Values of 1.4 micrograms and above were observed in newly born infants, in normal adults with mild bilirubinemia and in persons with icterus due to cirrhosis of the liver. Low values were observed in barbital poisoning, nephritis with edema, leukemia, pulmonary tuberculosis and diabetes.

The average copper content of the serum of normal persons was 0.8 and 0.92 microgram per cubic centimeter in young men and young women respectively. Values of 2 micrograms per cubic centimeter and above were found in pregnancy, at term and in advanced carcinoma. Markedly low levels were observed in the serum of newly born infants. Intermediate values were observed in a variety of diseases.

Speculations are offered concerning the probable existence of different types of disturbances of the "copper-iron picture." GUEST, Cincinnati.

THE USE OF AN INTRADERMAL TEST IN THE DIAGNOSIS OF TRICHINIASIS. O. R. MCCOY, J. J. MILLER, JR., and R. D. FRIEDLANDER, J. Immunol. **24**:1 (Jan.) 1933.

The authors tested a large series of patients with trichinosis and a much larger series with controls of various types. The test consists in the intradermal injection of a solution of pulverized dried Trichinella larvae. The details for preparing the antigen are given in the text. A positive reaction consists of the immediate formation of a wheal surrounded by a zone of erythema.

About 90 per cent of persons ill with trichinosis give a positive reaction when the disease is well established, usually from two to three weeks after infection. There is a tendency for the skin to lose its sensitivity over a period of years following infection.

A high percentage of patients infected with Trichuris trichiura react to trichinella antigen. The authors interpret this as being a biologic group reaction. However, a more concentrated antigen was usually required to elicit a reaction in trichuris infections than in trichinosis.

The authors conclude that from a practical standpoint the intradermal test cannot be considered a certain diagnostic test. A negative test may be of more value in ruling out a diagnosis of trichinosis than a positive one in establishing it. A positive test justifies further search for the parasite.

FOTHERGILL, Boston.

A NEW METHOD OF STUDYING EDEMA. F. H. LASHMET, J. Michigan M. Soc. **31**:114 (Feb.) 1932.

Lashmet states that the usual methods of measuring edema by the correlation of changes in body weight with differences in fluid intake and output are often fallacious. There are five different possibilities for gain in body weight, as follows: tissue gain, edema gain, tissue and edema gain, edema gain greater than tissue loss or tissue gain greater than edema loss. He details a plan for measuring actual values and differences for these factors, based on exact knowledge of ingoing and outgoing calories, as well as ingoing fluid (drink, food, oxidation and "preformed" water) and outgoing fluid (urine, stool and vapor from lungs and skin). The application of the method to a patient is shown.

SMITH, Ann Arbor, Mich.

ALLERGIC DISEASES IN CHILDREN. S. J. LEVIN, J. Michigan M. Soc. **31**:116 (Feb.) 1932.

The general facts of the accepted allergic conditions are discussed. Diagnosis may rest on a typical symptom complex, a family history of allergy, other allergic manifestations in the patient, alleviation of symptoms on the removal of a certain substance and an eosinophilia in active manifestations. Intradermal tests are advised to supplement scratch tests. They should be done with caution. Group tests are unsatisfactory. A careful family and individual history are essential.

In 30 per cent of the cases of eczema, wheat, milk or egg may be shown to be the exciting cause, though the origins of substances used in milk modification, such as corn, wheat, barley and cane and beet sugars, must be considered. In patients sensitive to milk, evaporated milk, soy bean milk, or milk boiled for an hour may be used. Babies may sometimes be desensitized by injections of milk. For the breast-fed infant, elimination of the offending substances (even cow's milk) from the mother's diet is preferable to weaning. Local treatment aimed particularly toward the prevention of secondary conditions of the scalp and fungous infections of the eczematous areas is advised. The author suggests injections of calcium gluconate in obstinate cases of urticaria and angioneurotic edema.

For asthma and allergic bronchitis it is important to rule out nonallergic causes of wheezing. It may be necessary to prevent infections of the upper respiratory tract which act as precipitating factors. The author feels that many cases of this sort are made worse by the indiscriminate removal of tonsils and adenoids. Hay fever and allergic rhinitis are best managed by desensitization, as is vernal conjunctivitis, if a specific agent is discoverable. If not, nonspecific protein therapy is recommended. In children who suffer from chronic colds the finding of an eosinophilia in the nasal secretions should lead to an attempt to manage the condition on a sensitization basis.

SMITH, Ann Arbor, Mich.

A CASE OF PRIMARY CARCINOMA OF THE LIVER IN AN INFANT. M. PIERSON and M. CAMPBELL, J. Michigan M. Soc. **31**:482 (July) 1932.

The authors report a case of primary carcinoma of the liver, probably of the bile duct type, first noted in a boy of 14 months. Though this is only the forty-fifth case in the collected literature, the authors give reasons for a belief that such neoplasms may be more common than this fact suggests.

SMITH, Ann Arbor, Mich.

ASCARIS LUMBRICOIDES INFESTATION IN CHILDREN IN OAKLAND COUNTY. H. R. ROEHM, J. Michigan M. Soc. **31**:531 (Aug.) 1932.

The percentage frequency of Ascaris infestation has been placed at 1.29 in New York (1920) and 1.96 in Chicago (1906). In a county in southern Michigan Roehm found a frequency of 1.75 per cent of living worms; however in only 0.58 per cent of the stools was a positive reaction for ova obtained. One hundred and seventy-one specimens of stools were examined. None of the three children with a positive reaction of the stools showed definite symptoms.

SMITH, Ann Arbor, Mich.

FALLACIES AND MERITS OF SENSITIZATION TESTS. G. L. WALDBOTT, J. Michigan M. Soc. **31**:698 (Nov.) 1932.

As common sources of error in the use of skin tests Waldbott lists the following: (1) the idea that the degree of cutaneous reactivity parallels clinical sensitization, and that the tests are necessarily the most important procedure in managing the allergic patient; (2) the frequency of negative tests in asthma of long duration, in old age, from old testing substances and when tests follow the administration of epinephrine or ephedrine, the assumption of a negative reaction when the reaction is delayed and the fact that tests with extracts of raw food substances may be negative while the cooked food produces a reaction; (3) the inconclusiveness of test substances containing histamine or similar material and of extracts from strongly concentrated foods, as well as from bacterial proteins; (4) the differences in reactivity of the skins of some persons and of various areas of the skin in the same person.

The positive test can be considered as an indication of past, present or future clinical sensitivity. As to technic, the scratch method, with fresh fluid extracts, is advised for general work. With insensitive skins, any reaction greater than others is to be noted. Passive transfer testing is sometimes necessary, while the patch test may be used in cases of dermatitis and conjunctival tests in pollen-sensitive patients with negative reactions of the skin. The history, food diary, elimination tests and observation of cases are always important. As to the test substances, it should be remembered that any substance, protein-containing or not, may cause allergic symptoms. Suggestions as to the more important ones are given.

SMITH, Ann Arbor, Mich.

THERAPEUTIC RADIOLOGY IN RELATION TO INFANCY AND CHILDHOOD. A. U. DESJARDINS, J. Michigan M. Soc. **31**:777 (Dec.) 1932.

This interesting and helpful article is opened with a general discussion of cell radiosensitivity. The author states that cells in general are more radiosensitive during youth than later. Cells are more responsive during mitosis than in resting periods. A description of the reaction of some of the more important body cell types is given. Structures made up chiefly of lymphoid cells are extremely sensitive, and after them come the salivary glands, testis and ovary, basal epithelium of the mucous membranes and skin, epithelium of the respiratory tract, endothelium of the blood vessels, pleura, peritoneum, connective tissue, muscle and bone; the least sensitive are adipose and nerve tissue. The crystalline lens is extremely sensitive before birth and during the first year. The same heightened sensitivity is also noted in the skin of the child as compared with that of the adult.

In eczema, dermatitis and ringworm, small doses at weekly intervals are recommended. In any period of three weeks the total dose should be less than the erythema dose. In eczema the roentgen rays should be used only after the acute stage of the process has subsided under topical applications. Ringworm of the scalp responds well to a dosage producing temporary alopecia. In the strawberry and cavernous angiomas, the response is better than in the port-wine type of birth-mark. The use of radium is advocated for such conditions, and directions are given. Directions for the irradiation of warts and keloid are also stated. It is stated that furuncles, abscesses and erysipelas often respond well to irradia-

tion, and for the last-named condition the roentgen rays are applied to the lesion and to a zone of normal-appearing surrounding tissue. Irradiation of the tonsils will inhibit the tendency toward hyperplasia, but surgical removal is advocated when a child has suffered repeatedly from tonsillitis. If irradiation is used, a transient and harmless swelling of the parotids may follow. In simple lymphadenitis, this treatment will be helpful if the primary focus has also been dealt with by the same or other means.

In tuberculous lymphadenitis, irradiation is advocated as the method of choice. Methods of application are given, and aspiration of fluctuant areas is advised, preceding this treatment. The more fresh lesions yield more readily than the older ones because they contain less connective tissue.

There is an excellent and conservative discussion of hyperplasia of the thymus and the occasion for irradiation of that structure. The author states that the value of irradiation in pertussis is uncertain and is apt to remain so until the etiology of the condition is clarified.

For acute leukemia in the first decade of life, the author opposes roentgenotherapy. In patients over 10, when the disease is less acute, small doses may be used over small areas, but "intensive irradiation has no place in the treatment of leukemia of any age." In Hodgkin's disease, the rapidity of involution of swellings under irradiation may be of diagnostic aid in doubtful cases. The author advocates the use of roentgen rays alone or with radium applied to all areas of lymphadenopathy in this condition, and feels that moderate anemia and leukopenia are indications rather than contraindications for such treatment.

The only benign neoplasm (if it is truly neoplastic) amenable to roentgenotherapy is the giant cell tumor of bone. Transient pain and swelling may follow treatment of these processes. Of malignant tumors, particularly the endothelial myeloma, the chondrosarcoma and Wilm's tumor of the kidney will retrogress under irradiation, which relieves symptoms and delays the outcome.

SMITH, Ann Arbor, Mich.

THYMIC DEATHS. HARRY M. GILKEY, J. Missouri M. A. **30**:1 (Jan.) 1933.

This article again calls attention to the fact that the thymus gland is an organ of the higher vertebrates, developing up to the time of maturity and undergoing retrogressive changes at that time.

In any illness lasting more than twenty-four hours the weight of the thymus is reduced regardless of the cause of death, except in cases of tumor of the thymus, leukemia and exophthalmic goiter. This involution is probably part of a general process of inanition including all lymphoid tissue and subcutaneous fat.

Of much greater importance than the occasional death due to status lymphaticus is the fact that milder grades of this lymphatic condition are commonly present and cause a weakened constitution that contributes to the ill health of a large number of people, particularly infants and children. Accompanying it are changes in the blood which lengthen coagulation time and decrease the percentage of polymorphonuclear cells and their power of responding to stimulation. The blood sugar is lowered.

The value of the Cin-ex camera in the study of the thymus, as reported by Hasley and DeTomasi, is emphasized. The two main factors that tend to give discrepancies in the ordinary roentgenogram, namely the respiratory and heart mechanisms, are eliminated by the Cin-ex camera studies.

The signs and symptoms noted as due to enlargement of the thymus are cyanosis, dyspnea, stridor (particularly inspiratory), projectile vomiting and convulsions.

BERGER, Kansas City, Mo.

DIABETIC CHILDREN. ELLIOTT P. JOSLIN, South. M. J. **26**:1 (Jan.) 1933.

Joslin points out the outstanding fact in the present status of diabetes, namely, that diabetic children are being kept alive. He states that one thousand children

represent the yearly accession to the children's diabetic population of the United States. He once more states his opinion that diabetic coma is preventable and that it is curable when it does occur.

Diabetic children maintain normal growth both mentally and physically, and in Joslin's series they tend to be above the average in both respects.

Arteriosclerosis does not now appear to the same extent that it did five years ago, but a high blood cholesterol is characteristic in the greater number of children who exhibit this condition. Complications, such as cataract and coma, are apt to be found in children in whom diabetes has been neglected.

The author discusses the influence of heredity in the transmission of diabetes and the prevention of the disease in the light of present knowledge regarding such heredity, pointing out, among other things, that 8 per cent of diabetic children are of Jewish parentage.

Diet, exercise and insulin are the three components of the diabetic regimen that are essential to successful treatment of the condition. These are discussed along with hypoglycemia and surgical procedures in these patients.

The paper is closed with a discussion of the value of summer camps for diabetic children.

SCHLUTZ, Chicago.

THE MEDICAL TREATMENT OF CONGENITAL PYLORIC STENOSIS. HUGH LESLIE MOORE, Texas State J. Med. **28**:459 (Nov.) 1932.

The author formerly found it necessary to resort to surgical treatment in about 75 per cent of the cases of congenital pyloric stenosis. Under newer methods of treatment he believes this percentage can be reversed, the surgeon being needed in only 25 per cent of cases. He reports six cases with marked stenosis presenting all of the classic symptoms. All the patients recovered, and only one had the Rammstedt operation. There were five boys and one girl in the series.

He divided the treatment into three parts: First, enough phenobarbital is given to lower the excitability of the vomiting center in the brain. All of the patients required one-fourth grain (0.16 Gm.) every three hours. This causes the baby to sleep practically all of the time. Atropine is also given every three hours, but three patients in this series could not take it because of atropine fever. Second, concentrated food of high caloric value is given in amounts sufficiently small that the stomach can retain them as they are gradually increased. While completely relaxed from phenobarbital the large majority of children cannot swallow the old thick cereal formula. Third, the amount of body fluids is maintained by giving 100 cc. of physiologic solution of sodium chloride by hypodermoclysis twice daily, this being necessary for ten days or two weeks. Leaving out any of these results in failure. Hospitalization is no longer than is required for the surgical treatment, and the nursing expense is much less.

The author reports six cases in detail.

MOORE, Dallas, Texas.

ON THE ASSOCIATION OF PULMONARY CHANGES WITH RHEUMATIC PERICARDITIS. G. T. COOK, Brit. J. Child. Dis. **29**:264 (Oct.-Dec.) 1932.

This study comprises thirteen cases of rheumatic pericarditis. Pulmonary signs developed in twelve of the patients, the signs being confined to the left base in seven. No roentgen examination was made of any of the patients. Clinically, a pericardial effusion was diagnosed in five of the thirteen cases and a pleural effusion in two, but no paracenteses were done. Three of the patients died, and an autopsy was performed on one. The pulmonary observations reported by Naish, Fraser, Eiman and Gouley, Paul, Findlay, Coombs, Briscoe and others are discussed.

The view is put forward that the pulmonary condition may be regarded as an active massive collapse of a portion of the lung due to reflex disturbance of the vagus and sympathetic innervation of the lung from inflammation of the pericardium.

LANGMANN, New York.

A Pedigree of Haemophilia. W. J. Rutherford, Brit. J. Child. Dis. **29**:276 (Oct.-Dec.) 1932.

Seven cases of hemophilia were known to have occurred in the descendants (at least sixty-six persons) of a common ancestress. The sex of fifty-four is recorded, there being twenty-one males and thirty-three females—the preponderance of females the author attributes to pure chance operating in a small selected population. There were fourteen fatalities during infancy. Of the fatal cases of convulsion, five of seven occurred in boys. It is suggested that in some of these cases of hemophilia intracranial hemorrhage may have developed.

Langmann, New York.

Chronic Rheumatic Joint Disease in General Practice. Philip Ellman, Brit. J. Phys. Med. **7**:115 (Oct.) 1932.

The first of two articles on this subject deals with the classification, pathology, symptoms and signs of chronic arthritis. The author recognizes two distinct groups: (*a*) the atrophic or toxic group of arthritis (corresponding to the so-called rheumatoid or infective type), and (*b*) the hypertrophic or degenerative group (corresponding to ostearthritis).

The characteristic features of these groups are summarized in tabulated form.

Hartman, Cleveland.

Chronic Rheumatic Joint Disease in General Practice. Philip Ellman, Brit. J. Phys. Med. **7**:135 (Nov.) 1932.

The treatment of chronic arthritis is discussed in the second of a series of two articles. Ellman emphasizes the necessity for accurate diagnosis and early treatment and the recognition of the local and systemic nature of the disease. He regulates the diet according to a definite plan, and uses insulin when there are wasting and anorexia. Little is said about drugs. The author has seen little benefit derived from the use of vaccines, and he uses nonspecific protein therapy only in certain acute forms. A large portion of the article is devoted to a description of physical methods, including hydrotherapy, light treatment and electrotherapy. Diathermy, massage, manipulative therapy and roentgen therapy are discussed.

Hartman, Cleveland.

Lipoid Nephrosis in Children; Report of Three Cases. P. Gauthier and M. Schoenau, Arch. de méd. d. enf. **36**:34 (Jan.) 1933.

An exhaustive report of three cases of nephrosis from the children's clinic of the University of Geneva, with detailed laboratory observations, is presented.

A boy, 4 years of age, with the essential manifestations of lipoid nephrosis was admitted for treatment on Nov. 17, 1931, and died on Nov. 27, 1931, of a streptococcic infection involving chiefly the peritoneal and pleural cavities. The second case occurred in a girl of 3½ years suffering from lipoid nephrosis, with generalized edema, albuminuria and cholesterolemia. On a diet rich in protein there was no improvement, and only slight amelioration was noted when she was given thyroid extract. A regimen restricted to milk was then instituted; the child contracted measles with extreme hyperpyrexia, and three weeks later she was dismissed from the hospital in a satisfactory condition. The third patient, a boy of 10, sustained an attack of hemorrhagic nephritis superimposed on a chronic case of nephrosis. An acute mastoid infection developed, for which he was operated on, and in the course of his long illness he also contracted tuberculosis, of the juvenile type. In this instance, theobromine was used, with excellent results.

In their comment on these histories, the writers point to the ease with which secondary infections may supervene in nephrosis, either from the disequilibrium

of the blood itself or from a general lowering of the defenses of the body. They also call attention to the beneficial effect of strong febrile reactions such as those produced by measles and mastoid disease in the two patients who recovered.

AMESSE, Denver.

LIPOID NEPHROSIS IN AN INFANT OF ELEVEN MONTHS. M. L. SALDUN, Arch. de méd. d. enf. **36**:40 (Jan.) 1933.

On account of the age of the patient this case is discussed at considerable length. The infant, previously in excellent health, presented edema of the eyelids at 9½ months; in a short time the ankles were swollen and general edema of the entire body followed. When the patient was examined at the Visca Hospital in Montevideo, in addition to the anasarca, the liver was found to be enlarged, and the spleen was palpable in spite of the abdominal distention; there was dulness at the base of each lung, posteriorly, but only a slight elevation of temperature. The urine showed enormous quantities of albumin, with many pus cells and granular and hyaline casts but few red cells. Examination of the blood demonstrated an increase of the urea nitrogen to 30.1 Gm. per liter. On the third day following admission, bilateral bronchopneumonia developed, with high temperature and convulsions, death ensuing two days later.

AMESSE, Denver.

NONTUBERCULOUS SPONTANEOUS PNEUMOTHORAX IN A CHILD. SUFFOCATIVE TYPE TERMINATED BY SUDDEN DEATH. J. CHABRUN AND JOSEPH, Bull. Soc. de pédiat. de Paris **30**:19 (Jan. 19) 1932.

A boy, 4 years old, was admitted to the hospital after a week of illness which was characterized by a high temperature, cough, dyspnea and anorexia. He had an area of pneumonia at the apex of the right lung and a pneumothorax on the left side. The heart was markedly displaced to the right. On a number of occasions his breathing became so labored that a needle was inserted into the left pleural cavity and retained there until the pressure was relieved and the child improved temporarily. In one of these severe suffocating spells he died suddenly. This was undoubtedly a case of ball-valve pneumothorax. The most probable cause of the condition here was either rupture of an area of emphysematous lung on the side opposite to the pneumonia or rupture of the visceral pleura over a tiny patch of consolidation on the surface of the left lung. The tuberculin test was negative. Necropsy was not performed.

BENJAMIN, Montreal, Canada.

OSTEOPERIOSTITIS OF THE HUMERUS IN A CHILD WITH INFANTILE PARALYSIS OF THE LEFT UPPER EXTREMITY. L. BABONNEIX AND A. MIGET, Bull. Soc. de pédiat. de Paris **30**:25 (Jan. 19) 1932.

A boy, 6 years old, who had had infantile paralysis at the age of 4, had a swelling over the left humerus which proved to be due to osteoperiostitis of unknown origin. The left upper extremity showed flaccid paralysis as a result of the infantile paralysis, and it is believed that this case supports the view that parts of the body affected by infantile paralysis constitute sites of predilection for other pathologic processes.

BENJAMIN, Montreal, Canada.

ANATOMIC VERIFICATION OF A CASE OF PRIMARY CARDIAC HYPERTROPHY IN AN INFANT. GAUTIER AND SCHERMAN, Bull. Soc. de pédiat. de Paris **30**:46 (Jan. 19) 1932.

A girl, 21 months old, was shown before the society some time previously as presenting a case of idiopathic cardiac hypertrophy. The child was well for several months, but then dyspnea, edema, cough and albuminuria developed. She died a few days after admission to the hospital. Necropsy revealed bronchopneumonia and a markedly hypertrophied heart with all the valves intact. Histologic examination of the myocardium showed no pathologic changes.

BENJAMIN, Montreal, Canada.

PYELITIS DUE TO FRIEDLÄNDER'S BACILLUS. ROGER VILLIÈRE, Bull. Soc. de pédiat. de Paris **30**:57 (Jan. 19) 1932.

A girl, 23 months old, had pyelitis apparently caused by Friedländer's bacillus, which was cultured from the urine. The child was very toxic and showed marked neurologic symptoms. Infection of the upper respiratory tract was present, which may have supplied the portal of entry for the Friedländer bacillus. A vaccine was prepared, and it is believed that repeated injections of this vaccine effected a cure.

BENJAMIN, Montreal, Canada.

PROBLEM OF HYPERTROPHIC STENOSIS OF INFANTS: ITS MANAGEMENT AND PROGNOSIS. H. R. PASS, Beitr. z. klin. Chir. **155**:383, 1932.

The author discusses the management of forty-one operative and twenty-five nonoperative cases. He thinks that the condition is due to primary hypertrophy of the musculature rather than neurogenic. The follow-up of twenty-five infants to early childhood did not reveal any neurologic or nervous problems. This follow-up of twenty-five patients from three and one-half months to four years after operation showed normal form and function of the stomach, clinically and roentgenologically.

The author states that the best results are obtained when physicians and surgeons work together. The mortality rate was from 4.5 to 4.8 per cent. The most important conclusion is that there is no need to fear gastro-intestinal disturbances such as ulcer and colitis in later years.

RUBIN, Boston.

TREATMENT OF ENURESIS AMONG CHILDREN. CURT NELKEN, Deutsche med. Wchnschr. **58**:2034 (Dec. 23) 1932.

There is a group of children who are nervous and irritable, who sleep superficially, have bad dreams, grind their teeth while asleep and, as one of their symptoms, also wet their beds. According to the author, it is a mistake to disturb the sleep of these poor sleepers by awakening them during the night for urination.

If they are cured by suggestion, they get rid of only the enuresis which is one of their many symptoms. These children, especially, are improved by calcium therapy, which decreases their general irritability. Nelken advises the administration of calcium chloride by mouth, in doses of about 15 grains (0.97 Gm.) three times a day. It is remarkable that not only does the enuresis cease, but the improvement in the general condition and appetite of the child parallels the lowering of the nervous irritability.

KERESZTURI, New York.

THE GLYCOGEN DISEASE AND HEPATIC INFANTILISM. EGON UNSHELM, Jahrb. f. Kinderh. **137**:257 (Dec.) 1932.

In two infants of the same family a large abdomen developed soon after birth, owing to massive increase in the size of the liver. Growth was greatly retarded; the skin was hairy; venectasia of the cheeks appeared, and there were also moderate secondary anemia, rickets and osteoporosis. Both infants had numerous infections; both died after apparently trivial infections. Large and variable amounts of diastase were excreted in the urine; the diastatic activity of the blood serum was above normal. In one case autopsy revealed a huge liver, containing 14.2 per cent glycogen; 45.9 per cent of the dry weight of the liver was glycogen. Considerable quantities of glycogen were present in the striated muscles, the heart, the basal ganglions and, to a lesser degree, the kidneys. The glycogen of the liver did not disappear to an appreciable degree when it was kept at refrigerator temperature for seven days. Nevertheless, the liver was found to contain more amylase than normal, capable of hydrolyzing soluble starch and added glycogen. It therefore appears that the disease is due not to an abnormal power of laying down stores of glycogen, but to an inability to mobilize it, and that the glycogen is in some manner, as yet unknown, protected from the glycogenase of the tissues

and blood. The author critically reviews the cases of von Gierke (*Beitr. z. path. Anat. u. z. allg. Path.* **82**:497, 1929; *Med. Klin.* **27**:576, 1931), which were the first to be described, and discusses the various other types of hepatic infantilism with disturbed carbohydrate metabolism, which can be distinguished more or less readily from the "glycogen disease."

CLAUSEN, Rochester, N. Y.

THE RIGA-FEDE DISEASE. MICHIO KASAHARA and KANAE NAGATANI, Jahrb. f. Kinderh. **137**:303 (Dec.) 1932.

Sublingual fibroma is fairly common in Osaka. It appears in infants from 6 to 12 months old, only after the eruption of the lower central incisors and only prior to weaning. Unless the tumor is large enough to interfere with nursing, there are no local or general symptoms. Well nourished infants may be affected. The proper treatment is excision. Nine patients showed nearly uniform histologic changes: hyperplastic or necrotic epithelium; submucosa infiltrated by cells, many of them eosinophils; dilated vessels, and an increase of connective tissue. There was moderate eosinophilia.

CLAUSEN, Rochester, N. Y.

JUVENILE ANGINA PECTORIS. STANISLAV MENTL, Časop. lék. česk. **70**:18 (Jan. 2) 1931.

The few cases reported have been of syphilitic origin. The author reports in detail a case of nonsyphilitic angina pectoris in a youth of 17 who had had anginal attacks since the age of 12 years. The clinical diagnosis was aortic and mitral insufficiency, rheumatic endocarditis, chronic pericarditis, angina pectoris, chronic nephritis and chronic appendicitis. The blood pressure in the right arm was usually about 30 mm. higher than that in the left, and at times as high as 200 mm. The attacks were aggravated by cold and relieved by heat applied to the left arm. After tonsillectomy all rheumatic manifestations cleared up, but the anginal pains came on periodically. Huchard collected eighty possible etiologic factors in angina pectoris. The important ones considered in this case are rheumatic aortitis, pericarditis, myocarditis, especially infarcts, chronic valvular heart disease and an associated effort syndrome. Syphilis, which is such an important factor in juvenile angina pectoris was definitely ruled out.

STULIK, Chicago.

CONGENITAL PYLORIC STENOSIS. J. SVEJCAR, Časop. lék. česk. **70**:737 (May 22) 1931.

The author discusses the history and the many theories of pyloric stenosis and pylorospasm. He considers the four cardinal symptoms of projectile vomiting, visible peristaltic waves, a palpable pyloric tumor and pseudo-obstipation. There is possibly a constitutional factor, as the condition is much more common in the Anglosaxon and Teutonic races and rare in Slavic and Latin peoples. In ten years the author discovered only six cases in his large clinic. Some authors report a familial tendency and an incidence as high as 90 per cent in males in some series. The rationale of various methods of treatment is discussed. The author considers the condition a congenital pyloric stenosis and the hypertrophy of muscle fibers as the only pathologic finding in uncomplicated cases.

STULIK, Chicago.

BLOOD PRESSURE IN PNEUMONIC CHILDREN AND ITS PROGNOSTIC SIGNIFICANCE. P. LIDZKA, Pediat. polska **9**:403, 1931.

Lidzka discusses normal blood pressure in children, giving the formula for each determination, and shows that the accuracy of determinations of blood pressure in children depends on many technical factors. His analysis of the determinations

of blood pressure in 420 pneumonic children as related to the outcome of the disease may be summarized in the following classification of patients:

Group 1, in whom the blood pressure was normal throughout the course of the disease: All these children got well.

Group 2, in whom the blood pressure, both systolic and diastolic, rose during the disease: These children also got well, although the condition of some of them was very serious.

Group 3, in whom the systolic pressure rose and the diastolic fell, while the pulse pressure increased: Fifty per cent of this group died.

Group 4, in whom the systolic and diastolic blood pressure fell: All these children died.

KRUPINSKI, Chicago.

A CASE OF CHRONIC POLYARTHRITIS IN A NURSLING (STILL'S DISEASE?). S. YANAGAWA, J. Pediat., Tokyo, Oct. 20, 1932, no. 389, p. 1885.

A 3 month old infant at the age of 20 days had shown a swelling of the right elbow joint, followed by a similar enlargement of the joints of the left elbow and the right knee. The Wassermann test was repeatedly negative, and there was no history of premature birth or of a miscarriage on the part of the mother. The Mantoux test was also negative. Examination revealed that the limbs were almost in a state of paralysis, except for the left leg, and the involved joints were apparently tender on pressure and passive movements. The fingers of the right arm were edematous, and the hand was held in adduction at the wrist joint. No evidence of fluid in these joints was demonstrable. The right leg was shorter than the left, and the greater trochanter on this side was more prominent than that on the left. This was found to be due to the congenital dislocation of the hip on this side. The patient was admitted to the hospital with the diagnosis of congenital dislocation of the hip (right) and of osteochondritis syphilitica. After hospitalization, he was found to have hypertrophy of the heart and changes in the epiphysis of one joint, and otitis media, inguinal hernia, secondary anemia and enlargement of the liver and spleen developed. The patient was treated with arsphenamine and liver extract, and was discharged two months after admission. The author believes that the clinical picture fits in best with that of chronic polyarthritis of Still's type. Syphilis was seriously considered, but evidence was against this diagnosis.

KATO, Chicago.

A CASE OF EMPYEMA DUE TO B. ENTERITIDIS (GAERTNER). T. SUZUKI, J. Pediat., Tokyo, Oct. 20, 1932, no. 389, p. 1909.

The author reports a case of empyema due to Bacillus enteritidis (Gaertner) in an infant 2 years and 6 months old. The pus in the chest was brownish red and contained much fibrin in lumps. The culture resulted in the demonstration of B. enteritidis on two occasions. The treatment consisted of repeated aspirations and irrigations. An autogenous vaccine was prepared, and nine injections were given.

The course was chronic, and the patient was discharged after three months in the hospital and is still being followed, as the condition is not completely cured.

KATO, Chicago.

Nervous Diseases

DIAGNOSIS OF EARLY POLIOMYELITIS. J. E. GORDAN, J. A. M. A. **99**:1043 (Sept. 24) 1932.

Early diagnosis of poliomyelitis protects public health by early isolation and affords the patient early treatment. Preparalytic poliomyelitis is a clinical entity which can be diagnosed with relative surety. The diagnosis depends on "a healthy clinical suspicion and a lumbar puncture." Stiffness of the neck, rigidity of the

spine and ataxic tremor are the most valuable signs. Unfortunately, some of the more common diseases of childhood are diagnosed as poliomyelitis without sufficient critical differentiation, leading to unsatisfactory management of these conditions and unnecessary alarm about the actual prevalence of poliomyelitis. Certain findings should discount the diagnosis of poliomyelitis and suggest some other condition: swelling of the affected extremity; cervical adenitis; a critically ill, comatose patient; high fever, particularly of the septic type; localized abdominal tenderness; prolonged illness with subsequent paralysis, and regional sensory disturbances with paralyses and convulsions. The cerebrospinal fluid is clear or slightly hazy, and under increased pressure. There is no fibrin web. The usual cell count is from 50 to 100, with equal distribution of myelogenous and lymphatic cells early or predominance of neutrophilic polymorphonuclears early and later marked predominance of lymphatic cells. The sugar content of the fluid is normal. While examination of the cerebrospinal fluid aids materially, it is by no means essential.

BONAR, Salt Lake City.

STREPTOCOCCIC MENINGITIS WITH INTRACAROTID TREATMENT AND RECOVERY. M. S. ERSNER and T. H. MENDELL, J. A. M. A. **99**:1596 (Nov. 5) 1932.

The mortality in streptococcic meningitis is notoriously high. Forty-six persons have been reported cured by various measures. Two more patients are reported cured following intracarotid treatment with acriflavine base and a colloidal solution of iodine. Mastoidectomy was performed in both instances. Blood transfusions, frequent lumbar taps, injection of antistreptococcic serum and cerebral dehydration were used as adjuncts to treatment.

BONAR, Salt Lake City.

EXPRESSION OF THE EMOTIONS IN A BLIND-DEAF CHILD. FLORENCE L. GOODENOUGH, J. Abnorm. & Social Psychol. **27**:328 (Oct.) 1932.

This paper deals with a study of the emotional behavior of a 10 year old girl who had been blind and deaf from birth. The child was selected because of her complete isolation from ordinary forms of social intercourse, making for behavior which may be regarded as the nearest approach to "native" reaction patterns. The girl was observed daily for a period of several weeks with reference to those aspects of behavior which fall under the head of "expressive" movements, that is, startled attention, delight, joy, anger, timidity and fear. From her observations, Goodenough is of the opinion, despite the tendency in recent years to minimize the importance of the "native" element in emotional behavior as compared with "learned reactions" acquired as the result of social experience, that the primary forms of "expressive" behavior are determined by native factors. "Although among persons with normal sensory equipment, the original reaction patterns may be so overlaid with a veneer of socially accepted forms of behavior that it is difficult to distinguish the native from the acquired, nevertheless, the essential similarity of many of the reactions of this child to those seen among normal children makes one willing to hazard a guess that the veneer is not so complete nor so impenetrable as many have supposed."

ABRAMSON, New York.

THE AMOUNT OF MOTILITY OF SEVENTY-THREE NEWBORN INFANTS. O. C. IRWIN, J. Comp. Psychol. **14**:415 (Dec.) 1932.

Observations were made on the amount of motility exhibited by seventy-three new-born infants 2 weeks old or less. Measurements were taken by means of the Pratt cabinet, a two dimensional stabilimeter, giving a relative measure of motility, and the polygraph. Motility was measured in terms of oscillations per minute of the polygraphic pens, and observations were taken between 2:30 and 5:45 in the afternoon. The results showed that all infants were active at some time during the experimental period, no infant remaining totally immobile for

the entire period. However, enormous individual differences in the amount of motility were noted, the infant of highest motility being about 290 times more active than the least active infant. Fluctuations in motility from one day to the next were not significant, but after a period of several days, changes in the amount of activity became apparent. The most significant change in the amount of motility occurred during the first four days of life, with no variation during the next four day period. Marked differences in motility were noted during waking and sleeping, the infants being about six times more active when awake than when asleep.

ABRAMSON, New York.

THE DISTRIBUTION OF THE AMOUNT OF MOTILITY IN YOUNG INFANTS BETWEEN TWO NURSING PERIODS. O. C. IRWIN, J. Comp. Psychol. **14**:429 (Dec.) 1932.

Continuous graphic records were made of the motility of seventy-three new-born infants who ranged in age from birth to 16 days. The infants were fed at 2 p. m. and at 6 p. m., and measurements were taken at 2:30 p. m. and at 5:45 p. m. The results indicate that motility in the infants was greater just before nursing than immediately after, the motility toward the end of the experiment being almost three times as great as at the beginning. In order to ascertain whether the waking state as such was the cause of the increased motility or whether hunger played the dominant rôle, fractional comparison was made with motility during the sleeping state. The amount of motility during sleep was found to vary little from period to period, whereas it increased steadily during the waking condition of the infants, until it was about nine or ten times its initial value. In view of this result, the investigators are of the opinion that hunger, rather than the waking state, is the primary causal factor in the gradually increasing motility of the new-born infants, reaching its height just before feeding time.

ABRAMSON, New York.

EQUILIBRIUM BETWEEN CEREBROSPINAL FLUID AND BLOOD PLASMA: V. OSMOTIC PRESSURE (FREEZING POINT DEPRESSION) OF HUMAN CEREBROSPINAL FLUID AND BLOOD SERUM. FRANK FREMONT-SMITH, GILES W. THOMAS, MARY ELIZABETH DAILEY and MARGARET P. CARROLL, Brain **54**:303 (Sept.) 1931.

Comparative freezing point determinations on simultaneous samples of blood serum and cerebrospinal fluid in ninety-four instances (on seventy-three patients) are reported. In forty-four of the seventy-one comparative determinations in nonmeningitic cases, the freezing point of the cerebrospinal fluid was the same as that of the serum within 0.005 C., confirming the views of Mestrezat and Teschler. In ten instances of meningitis, the difference between the freezing point of the blood serum and that of the cerebrospinal fluid was greater than 0.025 C. This evidence helps to corroborate the thesis that the cerebrospinal fluid is a dialysate in osmotic equilibrium with the blood plasma.

MICHAELS, Boston. [ARCH. NEUROL. & PSYCHIAT.]

THE DELINQUENT CHILD. J. W. K. BRUCE, M. J. Australia **2**:647 (Nov. 26) 1932.

Bruce concludes that there is no single cause of delinquency. Certain factors may predominate — physical, environmental, intellectual and inherited ones and mental conflicts. The major factor is always combined with one or more other of the aforementioned causes as minor factors. A fall from 30 to 20 in the percentage of persons who relapse during the past two years is attributed to work performed in the clinic, improved magisterial methods of dealing with boys, constant efforts of the probation officers, and the cooperation of the medical profession, outside organizations and individuals.

GONCE, Madison, Wis.

SIGNS AND SYMPTOMS OF THE ACUTE STAGE OF ANTERIOR POLIOMYELITIS IN THE 1931-1932 EPIDEMIC. S. F. MCDONALD, M. J. Australia **1**:1 (Jan. 7) 1933.

McDonald gives a description of the clinical manifestations of poliomyelitis based on personal experience acquired in the Brisbane epidemic of 1931-1932. The most constant signs were rigidity of the neck and spinal rigidity. Amoss' sign was rarely positive. Muscle tenderness was uncommon until after paralysis had appeared. Tremor was not a prominent symptom. The spinal fluid cell count was proportional to the severity of the infection. Lumbar puncture was made with the patient under a general anesthetic. Older children were more seriously crippled than younger ones. Fatal cases fell into two groups: (1) the type in which there was overwhelming toxemia, usually with cerebral manifestations and a low cell count, and (2) the ascending Landry type, in which there was usually a high cell count.

GONCE, Madison, Wis.

SERUM TREATMENT OF ACUTE ANTERIOR POLIOMYELITIS. A. E. PATERSON, M. J. Australia **1**:5 (Jan. 7) 1933.

For the treatment of infantile paralysis Paterson advises convalescent serum in the dosage of 20 cc. intraspinally and 30 cc. intravenously. From a study of seventy-four cases, he has gained the opinion that a profound general reaction to the convalescent serum is beneficial; in his experience such a reaction has always been followed in about twelve hours by a sudden and striking improvement in the clinical picture of the patient. He also observes that spinal rigidity is apt to be gradual in its disappearance after the administration of convalescent serum.

GONCE, Madison, Wis.

TREATMENT OF ANTERIOR POLIOMYELITIS FROM THE ONSET OF PARALYSIS TILL THE END OF SPONTANEOUS RECOVERY OF POWER IN THE MUSCLES. L. W. N. GIBSON, M. J. Australia **1**:8 (Jan. 7) 1933.

Gibson emphasizes the importance of mental as well as of physical rest in the treatment of poliomyelitis in the acute and the subacute stages. Complete muscular rest of the trunk and legs in the early paralytic stage is brought about by the application of a complete plaster cast extending from the chest to the toes, which is later halved, and rest of the muscles of the arm is gained by the use of abduction splints of the type used in cases of birth palsy. Treatment of the convalescent stage calls for: (1) immobilization of the patient's limbs and trunk in such a way that the weakened or paralyzed muscles are placed in a position of relaxation, and (2) the institution of muscle training under the supervision of a skilled masseuse. Gibson observes that the degree of muscular tenderness may be used as a prognostic sign — the less the tenderness the more rapid the recovery.

GONCE, Madison, Wis.

LATE TREATMENT OF ANTERIOR POLIOMYELITIS. A. V. MEEHAN, M. J. Australia **1**:10 (Jan. 7) 1933.

Meehan discusses the various orthopedic methods of treating paralyses of the various parts of the body.

GONCE, Madison, Wis.

THE PATHOLOGY OF ACUTE POLIOMYELITIS. J. V. DUHIG, M. J. Australia **1**:14 (Jan. 7) 1933.

Duhig gives an excellent review of the literature on the following aspects of poliomyelitis: cause, epidemiology, portal of entry, propagation of the virus, pathologic anatomy, production of immune serum in animals with crude, partially or wholly neutralized virus, effectiveness of the convalescent serum, collection of convalescent serum, and route of administration of the convalescent serum.

GONCE, Madison, Wis.

EPIDEMIOLOGY OF ANTERIOR POLIOMYELITIS, WITH SPECIAL REFERENCE TO THE QUEENSLAND EPIDEMIC, 1931 TO 1932. J. G. DREW, M. J. Australia **1**:26 (Jan. 7) 1933.

The morbidity rates for 1931-1932 were 39.7 per hundred thousand in Brisbane and 28.6 per hundred thousand for the rest of the state. The fatality rate was 14.68 per cent and the death rate was 4.5 per hundred thousand of population. Sex had no influence on the incidence of the disease. The most common age of incidence was from 1 to 5 years in Brisbane and from 2 to 7 years outside the metropolitan area. Peaks of the epidemic were reached in spells of dry, warm weather. Dust, insects, food and the character of sanitation had no influence on the spread of the disease. The period of incubation was only one day in several instances. The disease spread definitely along the lines of communication and broke out for the first time in fresh communities among those in contact with persons who had arrived from a heavily infected area. Widely spaced dentition was present in many cases of the disease.

GONCE, Madison, Wis.

A REPORT OF THE EPIDEMIC OF POLIOMYELITIS IN NEW SOUTH WALES, 1931-1932. A. H. ZEBBOTT and K. HELMS, M. J. Australia **1**:43 (Jan. 14) 1933.

Four hundred and thirty-five cases of poliomyelitis occurred in New South Wales in the summer and autumn of 1931-1932. The epidemic started and reached its height earlier in Sydney than it did in the rest of the state. The mortality rate was 11.7 per cent in Sydney and 13.1 per cent for the whole state. The 214 cases which occurred in the metropolitan area were studied by the authors, and their report covers the following aspects of the disease: social environment, multiple cases in the same house, age incidence, sex incidence, clinical types of the disease, types of onset, symptomatology, the cerebrospinal fluid changes, the blood leukocyte count, differential diagnosis, and prognosis and treatment in the acute stage. Although patients treated with convalescent serum in the preparalytic and early paralytic stage seemed to be benefited by the serum, as determined by the absence or extent of paralysis in the acute stage, after one month and after six months, they were not compared with similar but untreated patients. The authors suggest that the diagnosis is made before paralysis occurs because there are usually (*a*) more significant symptoms, (*b*) more significant symptoms for a longer period, or (*c*) merely a longer preparalytic stage.

GONCE, Madison.

THE RECENT EPIDEMIC OF POLIOMYELITIS FROM THE PHYSICIAN'S POINT OF VIEW. E. H. M. STEPHEN, M. J. Australia **1**:60 (Jan. 14) 1933.

The author gives a good discussion of the symptoms and signs of poliomyelitis. He believes that convalescent serum is of definite value in the treatment of the disease.

GONCE, Madison.

SYNDROME OF VOMITING WITH ACETONEMIA IN MENINGOCOCCIC MENINGITIS AND TUBERCULOUS MENINGITIS. P. NOBÉCOURT, Progrès méd., Jan. 21, 1933, p. 110.

The clinical histories of cases of vomiting with acetonemia in meningococcic meningitis and in tuberculous meningitis are given. The cause of this complication is unknown. The syndrome must be divided into two groups: first, the common or cyclic vomiting and, second, the encephalomeningeal form, which may be due to the meningeal disorders described.

SANFORD, Chicago.

VASOMOTOR REFLEXES IN NEW-BORN AND NURSING INFANTS INSTIGATED BY STIMULATION OF THE SENSE OF TASTE. M. GALLUCCI, Riv. di clin. pediat. **30**:1396 (Nov.) 1932.

A plethysmograph, in which the baby's hand was placed and which was connected through a tambour to make a record on a smoked drum, served in the detection of vasomotor changes.

The new-born child shows a marked general reaction to food, but it was impossible to evaluate whether or not there is a vasomotor reaction. The new-born child shows no vasomotor reflex from the other sensory stimuli (touch, temperature or hearing).

At 15 days of age, the baby's vasomotor system reacts to touch and temperature.

In infants from 2 months to 1 year of age, stimuli of taste are constantly followed by vascular reflexes, even in subjects plethysmographically inactive to other stimuli. The taste stimuli were produced by giving the baby breast milk, cow's milk, dried milk, or a solution of sugar.

HIGGINS, Boston.

THE SPINAL FLUID IN CHILDREN. KURT SAMSON, Ergebn. d. inn. Med. u. Kinderh. **41**:551, 1931.

Examination of the spinal fluid of two hundred normal children between the ages of 6 months and twelve years gave the following results: In 80 per cent of the patients there were up to 5 cells per cubic millimeter; in 15 per cent, from 5 to 8 cells, and in 5 per cent, from 9 to 10 cells.

The higher cell counts were usually found in the younger children. The cells were practically exclusively small lymphocytes; polymorphonuclear leukocytes were never found in the normal fluids.

The Nonne-Apelt-Schumm as well as the Weichbrodt test for albumin always gave negative results; the Pandy reaction was negative in 95 per cent and faintly positive in 5 per cent of normal children. The colloidal gold reaction was negative. The sugar values ranged between 55 and 70 mg. per hundred cubic centimeters; 70 per cent of the patients showed from 60 to 65 mg.; 15 per cent, from 55 to 60 mg., and 15 per cent from 65 to 70 mg. The sodium chloride content was between 690 and 725 mg. per hundred cubic centimeters.

In the first half year of life there were in the spinal fluid certain deviations from the aforementioned data, which should be understood lest they be considered abnormal. The author first emphasized the frequency with which dry taps are encountered during the first fourteen days of life; this occurred in 15 per cent of his cases. The spinal fluid of full-term infants in the first eight days of life was constantly yellowish, although the intensity varied; the specimens of spinal fluid that were most colored gave a positive reaction to the Diazo test for bilirubin. The most intensely yellow specimens of spinal fluid were found in jaundiced infants. The cell count was from 3 to 20 cells per cubic centimeter, and there was a consistent increase in the amounts of albumin and globulin. The sugar content was between 30 and 70 mg., in most cases being lower than in later childhood.

The spinal fluid of premature babies was more intensely yellow, and the color persisted longer than in full-term infants, usually up to the end of the second week. The cell count and the albumin were somewhat higher than in full-term infants.

The author then reviews at great length the observations on the spinal fluid in various pathologic conditions in childhood, but he adds nothing new to the sum of information on the subject.

CAPPER, Philadelphia.

OBSERVATIONS IN REPEATED EPIDEMICS OF POLIOMYELITIS. W. POCKELS, Monatschr. f. Kinderh. **55**:259 (Jan.) 1933.

The writer compared the epidemics of poliomyelitis occurring in Frankfurt in 1913, in 1924 and in 1931. He also contrasted these with the epidemics in New York and Chicago. The epidemics in Frankfurt did not vary from each other in type or from those seen in this country.

The period of incubation ranged from eight to ten days. Contagion seemed to be by human contact. No relation could be established between the incidence of the disease and the height of the ground water or meteorologic conditions. Although the disease occurred in summer, the epidemics did not necessarily take place at times of the highest temperature.

GERSTLEY, Chicago.

INFECTIOUS ENCEPHALITIS IN CHILDHOOD. P. EIWIN and S. WURMAN, Monatschr. f. Kinderh. **55**:365 (Jan.) 1933.

The writers call attention to the increasing number of cases of infectious encephalitis occurring in the last ten years. This complication may occur during any infectious disease independent of its form and severity. The clinical picture differs from that in adults in that the symptoms are manifold and result more frequently from lesions of the extrapyramidal tract. More frequently, symptoms resemble those of meningitis with convulsions. Change of muscle tonus is also frequent. The prognosis is highly indefinite.

GERSTLEY, Chicago.

BIOPHYSICAL CONSTANTS OF CONSTITUTION: TESTS OF THE VEGETATIVE NERVOUS SYSTEM. S. EDERER and E. KERPEL-FRONIUS, Monatschr. f. Kinderh. **55**:417 (Jan.) 1933.

In an effort to obtain measurements for types of constitution, the writers used blood pressure tracings as influenced by eliciting the oculocardiac reflex. They obtained reactions rather typical for certain types of constitution. Contrasting curves are shown for the vagotonic and the sympathicotonic person. The authors discuss these curves with reference to the height of the reaction, duration phase, latent period, irritability of the system, weakening or intensifying of the reaction during the experiment and changes in the reaction following stimulation.

GERSTLEY, Chicago.

Diseases of the Eye

THE EYES OF SCHOOL CHILDREN. E. JACKSON, Am. J. Ophth. **15**:901 (Oct.) 1932.

The author outlines the procedure for a complete examination of the eyes of school children. He describes the method of determining the visual acuity demonstrated by Brown and Royer and emphasizes its practicability. Next in importance is the ophthalmoscopic examination. Skiascopy, without cycloplegia, rapidly gives information of real value, revealing any gross heterophoria or weakness of ocular movement that calls for attention. If there is any reason to suspect that the field of vision may be defective, the best test is the confrontation test, in which the child is required to tell whether the fingers are held still or are moving in the periphery of the field.

ZENTMAYER, Philadelphia. [ARCH. OPHTH.]

A CASE OF CONGENITAL CATARACT SHOWING UNUSUAL FEATURES. D. J. WOOD, Brit. J. Ophth. **17**:158 (March) 1933.

The patient was a Swahili boy. In each eye in the center of the dilated pupil was a dense circle of capsular opacity, with a yellowish raised epicapsular spot and several smaller specks, remains of lens matter. The central dense part was marked by concentric lines, which were rather bluish and tendinous looking in the right eye. Around this central opacity was a flat, slate-colored band, notched at its inner margin and furrowed on its surface. This represented a thinner part of the capsule, with an impress of the uvea through which the dark interior was dimly seen.

The central part was separated, leaving a round disk of capsule on the anterior chamber. This was later removed, resulting in a clear space through which with glasses good vision was obtained.

Microscopic examination of the disk of capsule showed the anterior surface marked by digitate wrinkles outlined by fine atoms of pigment and the posterior surface marked with concentric wrinkles with oval nuclei lying in lines corresponding to them. No nuclei belonging to the anterior capsule were visible.

ZENTMAYER, Philadelphia. [ARCH. OPHTH.]

SIGHT-SAVING CLASSES. N. BISHOP HARMAN, Brit. M. J. **1**:129 (Jan. 28) 1933.

Harman finds that the ocular defects of children in sight-saving classes fall into three groups: myopia, 62.6 per cent; damages due to inflammation, 30.4 per cent, and congenital defects, 7 per cent. The presence of persons with the defects in the last two groups complicates the curriculum, since they are not of the same standard of intelligence and capacity as the patients with myopia, but an increase in the number of classes helps to reduce the difficulties.

The author believes that prolonged close work is a cause or an aggravation of myopia. In Sweden, classical studies which require close attention to books and the frequent use of dictionaries are eliminated. Harman previously reported that among 480 persons between 20 and 60 years of age with myopia of more than 3 diopters, 53 per cent of those engaged in close work eventually were unable to continue work because of serious eyestrain and 15 per cent suffered injury to the eyes. According to the degree of myopia, he obtained these results: myopia from 3 to 5 diopters, breakdowns 33.7 per cent; from 5 to 10 diopters, breakdowns 66.5 per cent; more than 10 diopters, breakdowns 77.4 per cent. Of children not engaged in continuous classwork, only 9.4 per cent experienced a critical loss of capacity as a result of eyestrain or disease.

Vision of at least 6/24 with glasses is necessary in these classes. Moreover, the relation of myopia to age is important; a child of 5 years with 5 diopters of myopia needs special treatment more than a child of 13 with 7 diopters, since the latter will leave school shortly.

At present, in the sight-saving classes there is 1 place for every 600 school children. Harman believes that the ratio should be 1 to 500.

The work in the class for persons with myopia is essentially personal and is of three types: (1) oral teaching, (2) written work and (3) handicraft. Only perfect natural lighting is used. Blackboards surround the room; there are continuous black screens on rollers, and the top of each desk is a full-sized blackboard. The oral lessons are taken with the normal children, and the written work is done in the special room on the blackboards. Mental arithmetic is stressed. Permanent records of work are made on large sheets of paper either by hand or by large rubber-faced type. The optical lantern is of little value because of the blurred images. Typewriting is not stressed, as it calls to mind a future clerkship. Printed books are not desirable, since it is desired to cultivate a habit of not reading.

Handicraft, which is the all in all of the blind school curriculum, is to the sight-saving class what Latin is to the public school, a training in care, precision and control. It trains the hands and the eyes and cultivates association.

Children from these classes are urged to choose outdoor work, work requiring standing and moving and a minimum of close work. Each school in London has voluntary helpers who attempt to direct the children into suitable work. All children receive periodic physical and ocular examinations, and detailed records are kept.

Children of exceptional ability have special classes in the higher schools, but if signs of eyestrain are found, they are removed at once. As a rule, the myopia remains unchanged over a period of years, and at the age of 16 or 17, selected students are allowed to take "leaving examinations." The mean average increase of myopia per annum has been about 0.2 diopter. The students take up salesmanship, domestic science, farming, nursing, massage and other suitable professions. In spite of efforts, about 2 per cent have taken up unsuitable work.

Harman believes that these classes offer a distinct advantage over the practice prevalent thirty years ago of forbidding attendance at school to highly myopic children.

DUGGAN, New York. [ARCH. OPHTH.]

PRIMARY TRACHOMATOUS INFECTION IN THE INFANT AND IN THE ADULT. TALBOT, Rev. internat. du trachome **10**:42 (Jan.) 1933.

Primary infection in infancy is the rule in trachoma, and the campaign of prophylaxis in endemic regions must be guided by this fact. Latent trachoma in the mother and in associates transmits the infection to the nursling and infant.

Trachoma in the adult is generally an attack of superinfection on the basis of a persisting latent disease. Since in northern Africa and the Levant less than 10 per cent of the girls attend schools, prophylactic attention must extend beyond these institutions and include infant-welfare stations and homes as well.

LEBENSOHN, Chicago. [ARCH. OPHTH.]

LYMPHOSARCOMA OF THE ORBIT OCCURRING SHORTLY AFTER ENUCLEATION FOR METASTATIC OPHTHALMIA. C. GALEAZZI, Arch. di ottal. **39**:454 (Sept.-Oct.) 1932.

A month after enucleation, in a boy 4 months old, swelling of the orbit and brow occurred. Diagnostic puncture revealed a large number of lymphocytes and lymphoblasts. Roentgen examination showed atrophy and erosion of the upper orbital margin. At operation an ill defined mass was found in the orbit and extending up onto the brow. The orbit was eviscerated. Sections showed a typical, very vascular lymphosarcoma. The child died three weeks after operation.

GIFFORD, Chicago. [ARCH. OPHTH.]

THE CLAUDE-BERNARD-HORNER SYNDROME IN CHILDREN: THREE CASES OF SYMPATHETIC OCULAR PARALYSIS FROM DIFFERENT CAUSES; HETEROCHROMIA OF THE IRIS ASSOCIATED WITH ONE CASE. C. COCCHI, Riv. di clin. pediat. **31**:641 (June) 1933.

The author reports three cases in which the Claude-Bernard-Horner syndrome was present. There are pictures of the three children, each showing the three features of the syndrome—the small pupil, the enophthalmos and the narrow opening of the lids; there is also pictured a dissection of the neck showing the course of the sympathetic nerve with the surrounding tissues.

In case 1, that of a baby of 7 months, the syndrome followed recurrent laryngitis with cervical and mediastinal adenitis; the tuberculin test was positive; the syndrome was still present when the child died at the age of 20 months.

In case 2, the child aspirated a metallic foreign body; the syndrome appeared with the development of mediastinal adenitis and empyema. With the removal of the foreign body and the recovery of the child, the syndrome disappeared.

In case 3, that of a girl, aged 9 years, the probable cause was an injury by forceps sustained at birth. A scar persisted on the neck near the location of the sympathetic nerve. The iris of the right eye, the involved eye, was blue-green; the iris of the left eye was chestnut brown. The father said that at birth both eyes were blue, but that the color of the left eye had gradually become darker, whereas the color of the right eye had not changed.

HIGGINS, Boston.

ENCEPHALOMYELITIS OPTICA ACUTA: REPORT OF A CASE. J. KLAR, Klin. Monatsbl. f. Augenh. **89**:645 (Nov.) 1932.

The author reports four cases of acute optic encephalomyelitis, a form of disseminated encephalomyelitis. This is a severe acute disease of the retrobulbar portion of the optic nerve, occurring first in one and then in the other eye. Choked disks usually cause total but transient amaurosis, resulting after weeks or months in recovery, with functional defects, which, however, may be missing occasionally. The ocular symptoms usually precede other manifestations of inflammatory disease of the central nervous system, e. g., of the optic tract, the chiasm, the pyramidal tract and the spinal medulla.

The patients included a girl, aged 13, two women, aged 27 and 32, and a woman, aged 37, who was pregnant. Among the ocular symptoms were noted binocular defects of the right lower quadrant of the field of vision, extending upward and downward in the periphery in the shape of a crescent in two patients, relative scotoma, homonymous hemiamblyopia for colors, visual deficiency and choked disks.

The author considers this combination of disturbances in the optic stem and optic tract valuable in differentiating acute optic encephalomyelitis from disseminated sclerosis. He thinks that the choked disks in his cases were not local inflammations but were caused by close proximity to the globes of the foci in the optic nerves. A disseminated disease of the central nervous system was evidenced by the absence of the Babinski, Gordon and Oppenheim reflexes, by anesthesia and analgesia of the dorsal segment and by paralysis of the bladder and the rectum. Furthermore, there were deflection of the tongue to the left side, clonic increase of the patellar, achilles, radial and triceps reflexes, paresthesias and twitching of the legs.

Increased pressure of the spinal fluid was found in none of the four cases, nor was exposure, injury, syphilis or any other infectious disease a possible etiologic factor. No information could be gained as to the possible immunity of the four patients to recurrences. The inflammatory nature of the disease seems to be established by the temperature curve, the positive reaction to globulin and a slight pleocytosis of the spinal fluid.

STOLL, Cincinnati. [ARCH. OPHTH.]

AN ANOMALY OF THE EYELASHES. K. HIROSE and M. HIRAYAMA, Acta Jap. Ophth. Soc. **36**:108 (Aug.) 1932.

A girl, aged 17, exhibited on the tarsal conjunctiva of the upper lid, 2 mm. posterior to the margin of the lid and a little to one side of the middle of the lid, a black hair, which was directed upward. The eyelids were otherwise normal. The hair, together with the surrounding tissue, was examined histologically; the hair was found to be an eyelash and represented an aberrant hair anlage.

KNAPP, New York. [ARCH. OPHTH.]

STATISTICAL STUDY ON TRACHOMA IN THE BRANCH SCHOOLS OF THE PEIPING NORMAL UNIVERSITY. S. P. CHANG, Nat. M. J. China **18**:958 (Oct.) 1932.

Among 2,528 students examined, 456 were found to be suffering from trachoma, that is, 12 per cent. Among 1,247 males examined, 19.7 per cent suffered from trachoma, while among 1,281 females, the percentage was 16.4. The percentage in regard to age showed that the chances of contagion increased with age. Under 10 years, the percentage was 7.2, while above 10 years, it was 28.9. Of the forms of trachoma, the papillary was predominant, and the cicatricial least seen.

MCKEE, Montreal, Canada. [ARCH. OPHTH.]

Diseases of the Ear, Nose and Throat

RADIOGRAPHIC STUDY OF THE NORMAL SINUSES IN INFANTS AND CHILDREN. CHARLES GILMORE KERLEY, Arch. Pediat. **50**:323 (May) 1933.

Attention is again called to the relative frequency of sinusitis in infants and young children. The author believes that transillumination will in many instances indicate sinusitis, but negative findings by transillumination do not exclude sinus disease, and roentgen examination should be made in suspected cases. The article contains illustrations which the author believes represent the normal sinuses at different ages of infancy and childhood.

WADDELL, JR., University, Va.

LARGE POSTNASAL POLYP IN A CHILD. IRVING WILSON VOORHEES, Arch. Pediat. **50**:367 (May) 1933.

The author reports the case of a large postnasal polyp in a child.

WADDELL, JR., University, Va.

FOREIGN BODIES IN THE AIR AND FOOD PASSAGES: REPORT BASED ON 334 CASES. PORTER P. VINSON, M. Clin. North America **16**:1471 (May) 1933.

In this series of cases, nuts of various kinds, including peanuts, were more frequently encountered than any other type of foreign body. Peanuts, however, did not present any greater problem than other vegetable substances. The location

of the foreign body was in the esophagus in 135 cases; in the right bronchus in 102; in the left bronchus in 56; in the trachea in 20; in the pharynx in 14; in the larynx in 6, and in a bronchus, the side not being designated, in 1. The esophagus is particularly intolerant to the presence of a foreign body, especially of a bone. In this location foreign bodies always produce symptoms; consequently they are seldom overlooked. In accord with the usual findings, males were the most frequent sufferers from this accident. Of the entire group of 328 patients, 165 were 5 years old or under.

Considerable divergence of opinion exists as to the advisability of general anesthesia in the operative treatment of patients with such cases. The author has been convinced, however, that local anesthesia or none is preferable in cases in which the foreign body is in the respiratory tract, but that ether anesthesia should be employed in cases of large foreign bodies in the esophagus in adults and in all cases of foreign bodies in the esophagus in children. Laryngeal edema is always a possible postoperative complication after bronchoscopy in children less than 7 years of age. When it occurs, tracheotomy is performed as soon as the breathing becomes definitely obstructed. Inhalations of steam appear to increase the edema. Oxygen, however, seems to be a valuable measure in preventing edema, and it is now given to all Vinson's patients under 5 years of age, immediately following bronchoscopic examination.

In 298 patients of this series, removal of the foreign body was followed by immediate benefit and, in most of them, by complete recovery. Death resulted in 16 cases, in 10 of which it followed the removal or attempts at removal of foreign bodies from the respiratory tract. In 6 cases death followed the impaction of foreign bodies in the esophagus.

SMITH, Ogden, Utah.

ARSPHENAMINE IN THE TREATMENT OF VINCENT'S ANGINA. ELIZABETH ANN SULLIVAN, New England J. Med. **208**:686 (March 30) 1933.

The treatment is of two types, local and general. Under local treatment many agents are used, such as tincture of iodine, sodium perborate, 10 per cent solution of silver nitrate, 6 per cent solution of zinc sulphate, 25 per cent solution of chromic acid and 1 per cent solution of copper sulphate and ethyl chloride applied to the lesions. General treatment consists of cod liver oil and tonics. For the specific action on the spirochetes, arsphenamine or similar preparations may be used intravenously and locally mixed with water or glycerin.

The author reports in detail the results obtained by these various methods in a schoolgirl, aged 12 years, in whom the symptoms continued for more than a month and recovery occurred after three days of treatment with arsphenamine intravenously and locally.

GENGENBACH, Denver.

EPIDEMIOLOGY OF SEPTIC SORE THROAT. PAUL B. BROOKS, New York State J. Med. **32**:1348 (Dec. 1) 1932.

Since 1925, 1,800 cases of milk-borne septic sore throat occurring in ten outbreaks have been recorded in the state of New York. In most instances these were traced to bovine mastitis. One of the largest outbreaks was traced to a thoroughbred cow in one of the best farms in the state.

The streptococcus causing the mastitis that ordinarily occurs in cattle is not usually harmful to man, but when injured udders become infected from human cases mastitis becomes responsible for epidemics. More cases occur among adults, and the deaths occur mostly in persons past middle age. Most of the cases occurring in persons under 15 years of age are in small children. "The only practical safeguard is pasteurization." Ordinarily there is little difference in the appearance of the throat in this condition and in scarlet fever.

AIKMAN, Rochester, N. Y.

REPORT OF SEPTIC SORE THROAT OUTBREAK IN GREENWICH, WASHINGTON COUNTY, N. Y. WILLIAM L. MUNSON, New York State J. Med. **32**:1351 (Dec. 1) 1932.

An explosive outbreak of twenty-four cases of septic sore throat was traced to a cow with one infected quarter. The farmer's wife had recovered from sore throat, and the farmer's throat showed hemolytic streptococci. The method of investigation of the epidemic is described.

AIKMAN, Rochester, N. Y.

SINUS DISEASE IN CHILDREN. V. W. FISCHBACH, West Virginia M. J. **29**:145 (April) 1933.

The prime object of this article is to emphasize the importance of careful and thorough study of the nasal sinuses of children with symptoms pointing to involvement of the head. Sixty-five per cent of the patients with chronic sinus infection give histories of repeated acute infections of the head in infancy. The remaining 35 per cent present histories showing contributory causes. Many patients with otitis media and with frequent colds are not relieved by removal of the tonsils and adenoids. Many cases of more general systemic infections are due to focal infections in the nasal sinuses. The primary cause of sinusitis is infection, but allergy, dietary factors and contact with chronic cases may be contributory causes. Examination, symptoms, diagnosis and treatment are discussed in detail.

SHAWKEY, Charleston, W. Va.

EYE, EAR, NOSE AND THROAT PATHOLOGY IN CHILDREN. A. P. HUDGINS, West Virginia M. J. **29**:160 (April) 1933.

The author makes an appeal for a thorough and complete examination in pathologic conditions of the eye, ear, nose and throat in children, with a search especially for obscure factors. It is not enough to assume, on the discovery of infected tonsils and adenoids, that therein lies the entire explanation of the patient's trouble.

The various pathologic conditions of the eyes, ears, nose and throat in children are discussed fully, together with their relation not only to each other, but to the more general and systemic infections. The importance of early, proper and persistent treatment of the primary foci is urged in order that the more serious secondary conditions may be avoided.

SHAWKEY, Charleston, W. Va.

THE TONSIL PROBLEM. AHTHUR K. HOGE, West Virginia M. J. **29**:170 (April) 1933.

This article deals with the problem of tonsillectomy in adults as well as in children. The results of tonsillectomy depend on the necessity for the operation and the careful selection of cases. Tonsils should not be removed during an acute infection or during an epidemic of acute disease of the respiratory tract, except possibly in an occasional emergency case. Tonsillectomy should be performed only by those who are proficient in the examination of the throat, who are familiar with the anatomy of the area and who have had sufficient surgical training to enable them to meet any emergency that may arise. The method of operation is of little importance so long as removal is complete and there is a minimum of trauma. All points of bleeding must be ligated, and the patient must be kept under careful observation until reaction from the anesthetic is complete.

SHAWKEY, Charleston, W. Va.

OTITIS MEDIA IN SUCKLINGS. W. M. MOLLISON, Brit. M. J. **2**:581 (Sept. 24) 1932.

The author considers infants in the first year of life as sucklings and calls attention to the fact that the British literature on the subject of otitis media during the first year of life is rather scant. From the discussion, one would gain

the impression that the examination of the ears with the otoscope as a routine measure is not common. Otitis media is classified as (1) obvious otitis media, with symptoms pointing to the ear; (2) latent otitis media, with no symptoms pointing to the ear, which includes (*a*) real otitis, discovered in infants apparently normal, and (*b*) pseudo-otitis, with general illness, crying, high temperature and refusal of food or with diarrhea and vomiting, or so-called parenteral disorders, and finally (3) tuberculous otitis media.

Symptoms and signs of obvious otitis media are outlined, and the treatment is described in more or less detail. Pneumococcic otitis media is emphasized, and its frequency is stressed. The author doubts that tuberculous otitis media occurs as often as has been indicated by some authors, but he states that when it does occur, it causes extensive destruction of the temporal bone with involvement of the glandular and facial nerves. When tuberculous otitis media is diagnosed, a thorough operation on the mastoid should be performed, and when this is done, there is a prospect of complete recovery.

ROYSTER, University, Va.

RECONDITIONING OF TONSILS BY THE DIATHERMY CURRENT. W. S. GROSS and BERNARD VARVILL, Brit. M. J. **1**:313 (Feb. 25) 1933.

The authors describe two types of tonsillitis. In the first type the tonsil is bright red, is covered by dilated blood vessels and has the appearance of acute inflammation. It is associated with a similar slight but definite enlargement of the cervical glands. The authors think that this type is usually caused by the hemolytic streptococcus. The second type is characterized by a rather pale, edematous or bluish appearance, with a definite bluish or dark red band on the anterior pillar. This, the authors think, is due to Streptococcus viridans.

Treatment with diathermy is given by a puncture method with a specially devised apparatus. The electricity is turned on, and this is followed by a whitish area and a loosening of the needle in situ. The average case requires six treatments at weekly intervals. There are marked atrophy of the tonsils in some instances and a general reconditioning, which, as the authors explain, improves the general condition of the patient.

ROYSTER, University, Va.

INFECTED TONSILS AS A SOURCE OF DAMAGE TO THE BODY. J. A. FIGUERAS, Arch. de med. inf. **1**:283 (Sept.) 1932.

Infections of the palatal or pharyngeal tonsils give entrance to the body to every variety of organism. These foci must be treated quickly by every available means. Surgical treatment is effective in most cases.

SANFORD, Chicago.

ROENTGENOTHERAPY IN CHRONIC TONSILLITIS. P. HESS, München. med. Wchnschr. **80**:384 (March 10) 1933.

For patients having chronic tonsillitis with recurring attacks of acute angina Hess found roentgenotherapy successful in giving permanent as well as immediate relief from symptoms. He was able to follow up thirty-one of his forty cases. The results were: permanently cured, 68 per cent; cured with recurrence, 10 per cent; improved, 12 per cent, and unchanged, 10 per cent. Surgical removal can be performed when the condition is not improved by roentgenotherapy. The operation is not more difficult than in previously untreated patients.

The beneficial effect of the roentgen rays is produced by destruction of lymphatic cells. The disintegrated cells stimulate the surrounding tissue to increased bactericidal activity, and in this way the infection is overcome. Hess gives the smallest dose of roentgen rays which will produce this effect without injuring the surrounding tissue. He used one-third erythema dose for the superficial tissues and one-fifth erythema dose for the deep tissues. The rays were directed from behind upward and mesially under the angle of the mandible. One treatment was given on each side on alternate days. The exposed tissues became swollen for a time after exposure. Recurrences can be treated by additional exposures.

BRAHDY, Mount Vernon, N. Y.

INVESTIGATION OF THE DEVELOPMENT OF SPEECH IN THE DEAF AND DUMB. KARL BALDRIAN, Ztschr. f. Kinderforsch. **41**:127 (Jan. 11) 1933.

Deaf and dumb children in learning to speak often show peculiarities which should be of great interest to the psychologist and philologist. The author believes that these peculiarities may throw considerable light on the psychology of the deaf and dumb. He discusses findings in three children whose intelligence was good and who had been under observation for several years.

REICHLE, Cleveland.

Surgery and Orthopedics

CAUSES OF ABSENCE OF OR RELATIVELY SLIGHT LEUKOCYTOSIS IN ACUTE APPENDICITIS. L. MÜLLER, Beitr. z. klin. Chir. **155**:467, 1932.

This is a study of 640 acute cases occurring between 1924 and 1929.

In fifty-two cases (8.1 per cent), there were white cell counts between 6,000 and 10,000. This group included cases with gangrene, peritonitis and formation of abscess. The author discovered that in these fifty-two cases, the majority of appendexes were found in hidden positions or surrounded by periappendical adhesions. These conditions prevent the involvement of the peritoneum in the inflammatory process. In these cases, the stimulation of the bone marrow even in destructive processes is light. Since the peritoneum is a sensitive membrane, even in mild infections, the white cells increase quickly.

RUBIN, Boston.

HEALING PROCESSES IN CONGENITAL DISLOCATION OF THE HIP. J. GANGLER, Beitr. z. klin. Chir. **155**:604, 1932.

The author comes to the conclusion, after observing and manipulating joints in cases of congenital dislocation of the hip, that it is perfectly permissible to leave the joint in immobilization for a long time after manipulation without worrying about the danger of relaxation. During the period of immobilization, the healing processes are already at work.

RUBIN, Boston.

SPONTANEOUS SUBLUXATION OF THE HIP JOINT IN THE COURSE OF ACUTE INFECTIONS IN CHILDREN. F. HOLLENBACH, Deutsche Ztschr. f. Chir. **237**:441 (Oct. 4) 1932.

The author described three cases seen during a period of four years in two boys of 6 and 9 years and a girl of 9 years. They occurred as the result of a metastatic coxitis in the course of severe generalized infections. The cause of the sepsis was mastoiditis in two cases and thrombophlebitis of the cavernous sinus in one case. In one instance the roentgenogram showed no abnormality of the joint other than the dislocation; in the other two cases definite destructive inflammatory changes could be demonstrated in the upper edge of the acetabular rim. These changes were, however, too slight to explain the subluxation, which in all cases was due to a rapidly developing extensive exudate into the joint, distending the capsule and displacing the head of the femur upward. The early destruction of the upper acetabular rim was doubtless favored by the passage of the head of the femur out of the acetabulum. In some cases the inflammatory process may proceed to such an extent that the acetabulum and the head of the femur are both destroyed. In the three cases described, resolution readily took place. In only one case, however, was the result satisfactory from the functional standpoint; in the other two cases there was severe bony destruction.

GLASER, Rochester, N. Y.

CARCINOMA IN CHILDREN. T. ECK, Deutsche Ztschr. f. Chir. **237**:450 (Oct. 4) 1932.

In children there is no significant difference in the sex incidence of cancer. The greater incidence in women over 30 is due to the frequency with which cancer attacks the female generative organs. The author described a case of carcinoma of the tongue in a girl 7 years of age, and stated that this is the first time such a condition has been reported in a person under 10 years of age. The paternal grandmother of the patient died of a carcinoma of the gallbladder. When she was about 6 years old the parents noticed a small, hard swelling in the middle of her tongue. Four weeks previous to the child's admission to the hospital the swelling increased in size and bled frequently. Biopsy showed squamous cell carcinoma. The entire growth was widely excised by electrocoagulation. The lymph nodes beneath the jaw were palpable and about the size of beans. Several of the nodes on the right side, which were somewhat larger than those on the left, were excised, but no evidence of metastasis was found. Three months later there was no evidence of recurrence of the carcinoma, and the ultimate prognosis was considered favorable. Postoperative radium or roentgen therapy was not employed. The author described three other instances of carcinoma in children seen in his clinic in the past twelve years: a gelatinous carcinoma of the rectum in a boy whose age was not stated; a carcinoma of the rectum in a girl 15 years of age, and a basal cell carcinoma involving the upper jaw of a girl 4 years of age.

GLASER, Rochester, N. Y.

SURGICAL TREATMENT OF EPISPADIAS IN THE MALE. S. FASSRAINER, Deutsche Ztschr. f. Chir. **237**:537 (Oct. *27*) 1932.

The difficulties of the surgical treatment of epispadias and the various procedures employed are reviewed. The author recommends as the first step the performance of a suprapubic cystostomy. A new urethra is formed by utilizing the sulcus of the urethra on the penis and a flap of skin and subcutaneous tissue from the adjacent abdominal wall. The skin of the penis, especially the foreskin, is mobilized to cover raw wound surfaces on the penis. If this procedure is employed, the author believes that it is possible to operate satisfactorily at an earlier age than is now the practice, and that because of this the normal growth and evolution of the genitals will be favorably influenced.

GLASER, Rochester, N. Y.

CARCINOMA OF THE ESOPHAGUS OCCURRING IN A CASE OF STRICTURE OF SIXTEEN YEARS' DURATION. H. HENNINGER, Deutsche Ztschr. f. Chir. **237**:632 (Oct. *27*) 1932.

The literature on this subject is briefly reviewed. The author states that less than 2 per cent of all carcinomas of the esophagus occur in persons under 30 years of age. In the patient described a stricture of the esophagus developed following the swallowing of lye at the age of 10 years. This necessitated the performance of a gastrostomy in order to feed the patient and dilate the stricture. The gastric fistula closed, and with the aid of occasional dilation by bougies the patient was able to swallow fluids and soft foods. At the age of 26 increasing difficulty in swallowing developed, necessitating frequent dilation of the esophagus, and he was admitted to the hospital during an attack of pneumonia. During the course of convalescence, while the stricture was being frequently dilated, the temperature suddenly rose and severe pain in the chest developed. The diagnosis was perforation of the esophagus with mediastinitis. The patient died, and at necropsy an ulcerating carcinoma of the esophagus was found at the site of an old stricture several fingerbreadths above the diaphragm. Pleuritis and mediastinitis were also present. The author believes that irritation of the stricture by means of the bougies probably played an important rôle in the development of the carcinoma.

GLASER, Rochester, N. Y.

Miscellaneous

AZTEC METHODS IN CHILD-TRAINING. JOHN RUHRÄH, Bull. Johns Hopkins Hosp. **52**:5 (Jan.) 1933.

Ruhräh has interested himself in the methods of child training as outlined in the third part of the "Codex Mendoza," which is in the Peabody Library. The "Codex Mendoza" is said to take its name from the viceroy of Mexico, who had it prepared by the Aztecs about the year 1540 to show the king of Spain something about the life and customs of his newly acquired people.

Several things stand out plainly, and these the Aztecs evidently regarded as the cardinal points in the education of children: (1) the avoidance of gormandizing and the careful regulation of food; (2) the avoidance of idleness; (3) strict punishment, and (4) vocational training.

LYTTLE, New York.

CARE OF THE BREAST DURING PREGNANCY AND PUERPERIUM. FRED EMMERT, J. Missouri M. A. **30**:155 (April) 1933.

Conditions which affect the activity of the breasts are given as the age and the parity of the mother, the environment, including hygiene and diet, the demands of the infant and his manner of nursing. Other conditions which may promote or depress the secretion of milk are pain from sore nipples or engorged breasts and, on the other hand, a satisfactory and pleasant nursing period.

Prenatal care of the breasts should consist only of daily washing of the nipples and areola with soap and water and protection against pressure, with a daily oiling with liquid petrolatum only during the last two months of pregnancy. In the case of inverted nipples, nipple aerators sewed into the brassière will help to evaginate them. Washing the nipple with alcohol and other astringents should be avoided. Manipulation of the nipple by the patient during this period may lead to infection and should be avoided.

Immediately after delivery the breasts are cleansed with soap and water and covered with a sterile towel. The baby is not brought to the breast for eight hours and then not oftener than once in six hours.

For engorgement of the breasts and for drying up of the breasts more or less routine procedures are advocated. In case of fissure, Ziegler's shields of lead or aluminum and cleanliness only are advocated.

Bardenheuer's operation is strongly recommended in case of abscess. This has the advantage that no glandular tissue or ducts are severed or destroyed, and the scar is masked.

BERGER, Kansas City, Mo.

INFANT MORTALITY: CAUSES OF DEATH DURING THE FIRST YEAR OF LIFE AS DETERMINED BY NECROPSY IN 517 CASES. JAMES B. GILLESPIE, J. Pediat. **2**:537 (May) 1933.

The primary cause of death in 517 infants under 1 year of age was obtained from the records made at autopsy in the department of pathology of the University of Minnesota during a period of three and a half years. The chief causes of death were: trauma at birth, 102 cases; premature birth, 97 cases; congenital malformations, 46 cases; pneumonia, 105 cases, and congenital syphilis, 8 cases.

LEMASTER, Evanston, Ill.

MEDICAL SUPERVISION OF NORMAL CHILDREN UNDER SCHOOL AGE: PRESENT EXTENT OF ITS APPLICATION. PHILIP VAN INGEN, New England J. Med. **208**:935 (May 4) 1933.

This paper is based on the results of the survey (already published) of preschool children made for the White House Conference on Child Health and Protection, with special reference to conditions in New England cities.

Interesting side-lights in the paper are the following observations: The lowest infant mortality occurs among American-born babies of Russian mothers, with babies of Scandinavian mothers next, of English, Scotch and Welsh mothers third, and of native-born mothers fourth.

In the utilization of health examinations, the children of Russian parents were first (65 per cent), and those of native-born parents second (52 per cent).

In vaccination against smallpox, Russian children were far ahead, with native-born children ninth in a group of eleven nationalities.

In immunization against diphtheria, Russian children were first, Italians second and native-born children eighth.

Russian children were also second in dental examinations.

GENGENBACH, Denver.

CHILD HEALTH CONFERENCES AND THE DOCTOR'S BREAD AND BUTTER. LEWIS WEBB HILL, New England J. Med. **208**:942 (May 4) 1933.

The author presents a very fair-minded, dispassionate opinion on this much debated subject. He believes that attendance at conferences on child health should be limited to families without income, those with an income sufficient only to provide shelter and meals, with no surplus for medical attention, and those able to pay moderate fees for illness but "with so little surplus that they do not wish to pay for medical attention when they are well."

Unfair to the medical man is the "come one, come all" attitude assumed by many nurses and social workers. Most unfortunate is the lack of interest displayed by the general practitioners, and even by some pediatricians, in preventive medicine, especially for the infant and child. The author presents a constructive program for use in private practice and suggests an ethical way of competing with the public clinics on the broad principle of "private service for those who can pay for it—public service for only those who cannot."

GENGENBACH, Denver.

CHANGES IN THE TEETH OF WHITE RATS GIVEN WATER FROM A MOTTLED ENAMEL AREA COMPARED WITH THOSE PRODUCED BY WATER CONTAINING SODIUM FLUORIDE. W. L. SEBRELL, H. T. DEAN, E. ELVORE and R. P. BREAUX, Pub. Health Rep. **48**:437 (April 28) 1933.

Drinking water containing 150 parts per million of sodium fluoride caused a loss of the normal orange color of the incisor teeth of white rats, followed by the appearance of irregular brown spots, similar to the changes produced by drinking water from an area where mottled enamel occurs. Water containing 500 parts per million of sodium fluoride was exceedingly toxic to young white rats and produced chalky-white, brittle teeth in those surviving the acute toxic effects.

LEMASTER, Evanston, Ill.

MATERNAL, FETAL AND NEONATAL MORTALITY AMONG 1,815 HOSPITALIZED AMERICAN INDIANS. E. BLANCHE STERLING, Pub. Health Rep. **48**:522 (May 19) 1933.

In 1,815 Indian women, the puerperal death rate and the neonatal death rate were lower than the rates reported for the United States in general. In this series 93 per cent of the deliveries were normal. There were twelve instances of twins.

LEMASTER, Evanston, Ill.

NATIONAL HEALTH POLICY: A CRITICAL SURVEY. J. L. BROWNLIE, Brit. M. J. **2**:275 (Aug. 12) 1933.

This paper is an address introductory to a general discussion on public health at the annual meeting of the British Medical Association.

ROYSTER, University, Va.

EXCRETION OF COLORED MATERIAL AFTER THE ADMINISTRATION OF CINCHOPHEN IN INFANCY. JULIUS SURANYI and EMIL VON LEDERER, Arch. f. Kinderh. **98**:178 (Jan. 24) 1933.

After the ingestion of cinchophen, sulphosalicylic acid added to the urine produces a green color. In older children excretion of a single dose is completed within twelve hours, but in infants the green color can still be produced in the urine twenty-four hours after the cinchophen has been given. The delayed excretion is a further indication of immature renal function in infancy.

LEMASTER, Evanston, Ill.

RESPIRATORY GYMNASTICS IN THE FORM OF PLAY. HELMUT HELMCHEN, Gesundhfürs. f. d. Kindesalt. **7**:350 (Nov.) 1932.

The importance of gymnastics in the treatment of static disorders of the spinal column and chest has long been recognized. The conventional form of gymnastics meets with at least passive resistance in the treatment of children. The author has, therefore, attempted to include the principles of these exercises in the form of games. The article is interesting, and the suggestions are ingenious.

REICHLE, Cleveland.

AN EXAMINATION OF THE MORBIDITY OF CHILDREN IN THE CHILDREN'S CLINIC OF DÜSSELDORF. WILHELM WIEDENFELD, Gesundhführs. f. d. Kindesalt. **7**:401 (Dec.) 1932.

This article is a statistical study of the types of disease observed in the Children's Hospital of Düsseldorf from 1907 until 1931. In general the same conclusions are reached from these observations as have been frequently observed in other parts of the world, namely, that the nutritional disorders have decreased greatly, that there has been a steady decrease in rickets, that there was a tremendous increase of tuberculosis during the period of war and inflation, and that there has been a steady increase in the number of premature infants.

REICHLE, Cleveland.

THE PHENOBARBITAL REACTION. FLESCH, Monatschr. f. Kinderh. **57**:321, 1933.

The author speaks of the good results obtained with phenobarbital in the treatment of chorea. The same results can be obtained with phenyl-ethyl-hydantoin. The advantage of phenobarbital is that it does not readily lead to the anaphylactic reaction (fever, exanthem and eosinophilia). In only one of a large number of cases of chorea was there such a reaction after treatment with phenobarbital. This was in a girl, aged 10 years, who received considerable amounts of the drug in the treatment for chorea. One year later, during a recurrence, phenobarbital was again ordered, and a scarlatiniform rash and fever lasting three or four days developed

GERSTLEY, Chicago.

PIONEERS OF SUMMER CAMPS FOR CHILDREN. S. LYSKAWINSKI, Zycie dziecka **1**:118 (June) 1932.

According to the author, the originator of summer camps for children was Walter Bion, a pastor from Zurich, Switzerland. Bion was born in 1830 and died in 1909. The first group of sixty-eight children was sent to the mountainous woods in 1876. This met with great success. The second instigator and organizer of summer camps in Europe was Stanley Markiewicz, a physician of Warsaw, Poland. He was born in 1839 and died in 1911. Both men deserve great credit for the work that they did in helping children physically through the summer camps.

KRUPINSKI, Chicago.

Society Transactions

CHICAGO PEDIATRIC SOCIETY

Regular Meeting, April 18, 1933

ARCHIBALD HOYNE, M.D., *President, in the Chair*

CHYLOUS ASCITES IN A NEW-BORN INFANT. DR. ANDERS WEIGAN.

A boy, born at full term on March 1, 1926, was the result of the second pregnancy of the mother. There was a normal spontaneous delivery under partial ether anesthesia. The resuscitation of the infant was prompt and normal. The birth weight was 10 pounds and 2 ounces (4,592.62 Gm.). The record made at the time of birth has this notation, "Abdomen distended and large; scrotum large." There were bilateral inguinal hernias and large inguinal rings. The meconium stool occurred within a few hours after birth.

The baby remained in the hospital for fourteen days; on leaving it weighed 10 pounds and 8 ounces (4,762.72 Gm.). The lowest weight was 9 pounds and 2 ounces (4,139.03 Gm.) when 48 hours old. Thereafter there was steady gain until the baby was discharged. He was breast fed and was given water frequently. He vomited often every day, and he had many stools. Enemas were given daily. On the fourth day the stools were yellow, and the infant was quite jaundiced. Enemas of barium sulphate were given on the second and the tenth days, as Hirschsprung's disease was considered a possibility. When the baby was discharged, the mother was requested to bring him back for observation.

After seven or eight days the mother returned the baby to the hospital because he had been restless and miserable; he had vomited and had been dyspneic; the abdomen had become more distended and tense; the skin of the lower part of the abdomen and the lower extremities was dark (the mother said, "almost black").

Dr. O. Theodore Roberg of the Swedish Covenant Hospital, who was attending the baby, asked Dr. Joseph Brennemann to consult with him because of the unusual condition present. Dr. Roberg and Dr. Brennemann advised an abdominal paracentesis, which was done. When the plunger in the trocar was withdrawn, a white milky fluid came out under pressure. About 2,000 cc. or more of the fluid was released; this immediately relieved the distention and dyspnea. Examination of the abdomen revealed no evidence of tumor or cysts, or of any other cause of the ascites.

The procedure was repeated a few days later and thereafter at intervals of from three to twelve days until the last aspiration, which was made on November 15, when the baby was 8½ months old. The shortest interval between punctures was three days. On one occasion the baby was not brought in for tapping for eleven or twelve days. On being questioned as to the reason, the mother informed us that she had given the baby more cereal feedings and a weaker milk mixture. The milky white fluid aspirated at that time seemed less dense than the fluid previously obtained, which had always been of practically the same consistency. The largest amount aspirated at any one time was 4,150 cc., on April 24; the smallest, 270 cc., on November 15. The usual amount aspirated ranged from 1,200 to 2,800 cc. There were, in all, thirty-five or thirty-six aspirations, totaling approximately 60 liters. Aspiration was performed eight times in September and seven times in October, which was more often than in any other month. The amount of fluid aspirated in September was 12,930 cc., and that in October, 8,290 cc.; the two aspirations made in November totaled 1,290 cc.

The criteria that guided the mother in bringing the baby to the hospital for tapping were discomfort and abdominal distention. The baby seemed to realize that the procedure would benefit him, and he was always a good patient. During this trying period the baby gained only 42 ounces (1,190.0 Gm.).

One chemical examination was made on May 12, by the Chicago Laboratory. The following report was given: The fluid aspirated from the abdomen amounted to 330 cc.; it was alkaline and milky; the specific gravity was 1.014; the total protein content was 1.8 per cent (albumin, 1.1 per cent; globulin, 0.7 per cent); the fat content was 0.1 per cent. It was said that the fluid was a transudate.

No cultures were made, and the baby had no evidence of any infection except in August, when he had an acute infection of the throat and diarrhea which lasted only a few days.

No Wassermann test was made, and there was no evidence of syphilis at any time either in the baby or in the mother.

There was a complete recovery, and both the inguinal hernias and the inguinal rings became normal. Tonsillectomy and circumcision were performed when the boy was 5 years of age. He is now 7, robust and healthy, and is attending school.

The condition was regarded as chylous ascites because: 1. The ascites was milk white and was discharged from the abdomen. A few clinicians, among them Goudine, assumed that all opaque white fluids from the abdomen or thorax are caused by a chylous admixture. 2. There was no evidence of any tumors or cysts at any time. 3. The condition was present at birth, and there was no history of injury to the mother ante partum. 4. The mother observed that reduced intake of fluid, especially of milk, influenced the amount of the ascites. 5. The infant's nutrition was poor. He gained only about 2½ pounds (921 Gm.) during the presence of the ascites, which lasted eight and a half months. 6. Frequent tappings brought about complete recovery.

The pathologic process is unknown, but there was probably an obstruction of the chylous ducts or collecting channels in the abdominal cavity. The disappearance of the ascites was possibly due (as suggested by Dr. Roberg) to the establishment of collateral chylous circulation.

CONGENITAL URETHRAL VALVES IN NEW-BORN TWINS. DR. MAXWELL P. BOROVSKY.

B. D., an octipara, aged 38, was delivered of twins on Nov. 8, 1932. She had not had twins previously. The delivery was uncomplicated. The infants, both boys, weighed 6 pounds and 1¾ ounces (2,771.15 Gm.) and 5 pounds and 12½ ounces (2,622.33 Gm.), respectively. Both had undescended testicles, but otherwise they appeared normal.

During the first few days of life, nothing unusual was noted in either of the twins. On the fifth day it was noted that the older one had edema of the lower part of the abdomen and showed an excessive gain in weight. The edema soon became more generalized and involved the tissues of the abdomen, the chest and the lower extremities.

Because of the good general condition of the infant and of the absence of other symptoms, this edema was at first thought to be due to some form of allergy. The urine was normal on the eighth day but showed a trace of albumin on the ninth day.

Two days later the second infant presented the same symptoms. The urinary bladder was found to be distended in both infants; it formed a globular mass extending above the umbilicus. Dribbling of urine was then noted, obviously a paradoxical incontinence.

At this time the urinary difficulty was considered to be caused by occult spina bifida, but roentgenograms of the lower part of the spine showed no abnormalities.

Catheterization was performed on the seventh day, and no obstruction was encountered. These catheterizations were repeated frequently for the relief of the distention of the bladder, each time with ease and success.

The edema became more generalized and included the face. On the seventh day twitchings of the upper extremities were noted. The feedings were taken fairly well, but there was occasional vomiting. The stools were rather frequent and loose. Pus appeared in the urine for the first time on the eleventh day.

The temperature, which had been normal or subnormal for the first eleven days, rose to 100.4 F. in the first child and to 101 F. in the second one on the twelfth day after birth, simultaneously with the appearance of pus in the urine.

Both infants showed a continued gain in weight, undoubtedly due to the generalized edema, but they began to lose weight rapidly on the fourteenth day. The

TABLE 1.—*Examination of the Blood on the Eighth Day of Life*

	Baby D. 1	Baby D. 2
Hemoglobin, per cent	95 (Sahli)	112 (Sahli)
Erythrocytes	4,900,000	5,670,000
Leukocytes	21,600	18,200
Color index	0.9	1
Differential count:		
Band forms	5	
Neutrophils	61	67
Small lymphocytes	28	27
Large lymphocytes	6	3
Monocytes	..	3

TABLE 2.—*Chemical Examination of the Blood* *

	Twelfth Day of Life		Fourteenth Day of Life	
	Baby D. 1	Baby D. 2	Baby D. 1	Baby D. 2
Sugar	60	71	91	100
Nonprotein nitrogen	128	120	117	137
Urea nitrogen	96.5	97	77.5	97
Uric acid	19.5	14	12.8	16
Creatinine	4.2	5.2	6	5.8
Plasma chlorides	560	370	500	400
Calcium	6			

* The results are given in milligrams per hundred cubic centimeters of whole blood.

TABLE 3.—*Chemical Examination of the Urine*

	Thirteenth Day of Life	
	Daby D. 1	Baby D. 2
Chlorides, per cent	0.026	0.26
Urea, per cent	4.7	3.68

intake of food became radically reduced, and the infants became drowsy and feeble. Dehydration, emaciation and circulatory collapse ensued, and the younger infant died on November 26, 1932; the death of the second twin followed in thirty-six hours. The clinical diagnosis was genito-urinary abnormality and uremia.

The course in both infants was identical as to onset, clinical picture, duration and termination.

Skiodan was injected intravenously on the twelfth day of life, one week after the onset of the symptoms, but there was no visualization in either infant probably because of the advanced destruction of the kidneys.

Autopsies were performed on both infants by Dr. I. Davidsohn. The following is a brief summary of the postmortem observations, which were almost identical in the two infants. There were marked hypertrophy of the bladder and obstruction of the posterior urethra by a pair of valves extending from the colliculus seminalis

anteriorly and acting according to the principle of one-way valves; i. e., antero-posterior passage of fluids was possible but postero-anterior passage was obstructed; the ureters were distended and tortuous; the kidneys showed pyonephrosis; pyelonephritis and suppurative perinephritis were present.

Early diagnosis and surgical intervention are the only hope for recovery in such cases.

DISCUSSION

DR. C. A. ALDRICH: Were the twins Dr. Borovsky described identical aside from their identical urologic lesions? I should also like to know whether he thinks that the destruction of the kidneys took place in utero or after birth.

DR. JOSEPH BRENNEMANN: There is one symptom that I think should be emphasized in connection with obstructions of the urethral vesical neck. I think that there is always a persistently distended bladder. We had a case recently in which the question arose as to whether the child had this trouble. Both the ureters were dilated, and there was a bilateral hydronephrosis. We decided correctly that the child did not have an obstruction of the vesical neck because the bladder was not distended.

I should also like to ask Dr. Borovsky whether the pyuria in these children was present before or after the first catheterization. In our experience pyuria results almost invariably after one intravesical manipulation if there is obstruction, that is, urinary stasis.

DR. MAXWELL P. BOROVSKY: The twins were identical in appearance and could not have been mistaken for anything but twins, even as new-born infants.

The question as to whether or not some pathologic condition of the kidney was present in utero I think can be answered only by the fact that the first urinalyses gave normal results. On the eighth day we found albumin, and on the twelfth day, pus. It is conceivable that some destruction of the kidney might have taken place before birth, since the bladder could not have become so markedly hypertrophied in the first few days of life. There probably was some destruction of the urinary tract, but we have no certain means of determining whether there was destruction of the kidney in utero or not, except that we found normal urine on the first examination, on the seventh day.

In many patients only partial obstruction is present, and children may have a mild urinary complaint but not marked obstruction of the urinary flow. If there is but partial obstruction, it is possible that the bladder partially empties itself.

The pyuria occurred three days after the first catheterization. Whether it was due to the catheterization or to further destruction of the kidney I cannot say. The bladder was constantly distended except following catheterization.

SITUS INVERSUS IN A DWARF. DR. JULIUS MEYER.

A boy, aged 9, first came under observation at the Pediatric Clinic at Northwestern University in March, 1932. The family history revealed nothing of importance. There was no history of any previous diseases. He was a full-term child, delivered by normal breech presentation; the weight at birth was 6 pounds (2,727.55 Gm.). He had been breast fed during the first six months, and then had received a mixed diet which included cod liver oil and orange juice. At 4 years of age he was markedly undersized. When seen at the clinic, his weight was 27¾ pounds (12,587.18 Gm.), and his height, 36 inches (91.44 cm.). He was small in all dimensions, symmetrical and fairly well proportioned, a miniature normal person.

The patient's dwarfism from that of the achondroplastic dwarf, in whom the head is abnormally large and the limbs are shorter than the trunk; it also differed from rachitic dwarfism, which is manifested by deformities of the limbs, from dwarfism due to organic disease, such as tuberculosis or syphilis, and from myxedematous dwarfism, in which there is retardation in mental and sexual development.

The basal metabolic rate was +2 per cent. A careful comparison of the metabolism of this boy with that of normal boys of the same age, height and weight showed no clinical or chemical evidence of an endocrine disturbance.

Congenital dextrocardia with complete situs inversus was revealed both by physical examination and by roentgenograms. The heart was on the right side, the aortic arch was toward the right, the liver was on the left and the spleen on the right, and the colon and the stomach would have appeared in transposed position had they been visualized. On examination, the sella turcica was first thought to be eroded, but on further investigation it was revealed to be normal. The anterior clinoid processes were well developed; they showed no evidence of erosions, and the floor of the sella turcica was intact.

The electrocardiogram of this child was studied under the direction of Dr. J. R. Miller; it showed a right axis deviation. The P (auricular) and T waves were inverted in the first lead. T_2 was flattened. There were deviation and complete inversion of P and T in lead I, but they were upright in lead III. Congenital dextrocardia with complete situs inversus is nearly always associated with reversal of all the waves in lead I. In this case, however, the electrocardiographic diagnosis was compatible with dextrocardia.

There was no evidence in the physical examination or clinical status of this boy to explain his failure to grow or to prove that he was suffering from any disturbance of the glands of internal secretion. The metabolic rate showed that he did not belong to the class of persons who have diminished glandular secretions, such as those with cretinism, hypothyroidism or myxedema, in whom the metabolism is lowered. He was a healthy boy who played as most children do except that his intelligence was probably slightly below par. He suffered very little handicap from the situs inversus but much from his dwarfism.

The normal, though miniature, proportions, together with the situs inversus, lead one to suspect that he was developmentally a twin, himself the mirror image of the other half of the fertilized ovum. The other presumably failed to develop after the original division.

Osseous Bands and Their Possible Relationship to Tuberculosis (Inaugural Thesis). Irwin Rubell.

Transverse bands in the long bones of children have been described by von Looser and others. Etiologically, they have been associated with rickets, scurvy, chronic debilitating diseases, anemias and malnutrition. Other factors are phosphorus or lead poisoning, hypothyroidism or constitutional inferiority. Pathologically, there is a retardation or cessation of cartilage proliferation, while calcification proceeds at a normal rate. This concentrates the bone-building energy of the shaft at a single level, producing the bands.

A boy, aged 9 years, had proved tuberculosis of the hip. Roentgenograms revealed osseous bands on all the bones of the body except in the skull. There were only three epiphyseal centers in the wrist, and in the ankle only those centers that normally ossify before the age of 3 showed the bands, while those that ossify at a later age did not show them. One may deduce from this that the interference with proper development of bone probably took place at or prior to the age of 3 years. Physical examination, laboratory studies and the history excluded any of the possible aforementioned etiologic factors. The only disease known to be present in this child was tuberculosis. It may be supposed that the primary infection took place sometime before the age of 3, and that the toxin produced a temporary cessation of cartilage proliferation with resulting band formation. While the cause and effect connection between the two conditions cannot be considered as proved, there is at least strong presumptive evidence that such a relationship may exist in this case.

DISCUSSION

Dr. Arthur H. Parmelee: About five years ago I presented before this society a child with hypothyroidism who had similar changes, as shown by roent-

genograms of the bones. The patient came under my care when she was 5 months old, and I have followed her course through a period of more than six years. I became much interested in this condition at that time, and in looking through the literature, I found a report by Getzky and Weihe in 1914, in which they described an identical case which occurred in a child with hypothyroidism.

Later I saw another child with definite hypothyroidism whose bones presented the same roentgenologic picture. A third patient seen by me a few years ago had this peculiarity in the growth of bone and was constitutionally inferior and mentally defective, but showed no certain signs of hypothyroidism. Then I saw a fourth patient, an infant of 5 months, with similar wide bands at the epiphyses of all the long bones. This child, though apparently properly fed and cared for, had never thrived, but there were no outward signs of hypothyroidism. I have not been able to follow this case since the child left the hospital.

Two years ago, in a 5 year old girl, a twin, lameness of one leg developed owing to an accident. Roentgen ray examination showed the transverse bands to be present on her long bones. I had roentgenograms made of the long bones of her twin sister, and, to my surprise, they showed the same condition. I had cared for these twins since birth. They had not had any severe illnesses, and they showed no evidence of hypothyroidism.

In 1929, Kemkes reported the case of a child of 5 years who showed transverse bands parallel to the epiphyses on all the long bones. Four other children in the family, including an infant who had not had cod liver oil or phosphorus, showed the same changes in the bones. There was no obvious evidence of hypothyroidism in any of these children.

A question arises as to the cause of this peculiar condition. If it were due to tuberculosis or to any of the ordinary infections, or to common diseases, we should expect to find the changes in the bones much more frequently than we do, unless, as seems probable, the condition is due to some peculiarity of the child itself.

During acute infections and in severe nutritional disturbances resulting from various causes, growth of bone temporarily ceases or is slowed up; a peculiar cartilage ground substance having an unusual affinity for calcium is produced in the zone of provisional cartilage calcification. This *Grenzscheide* makes border stripes, and when growth again goes on in a normal manner, these overcalcified areas are left behind on the shaft parallel to the epiphyses as fine transverse bands. This is what we commonly see as the result of illness. But in the case here reported, and in those I have mentioned, the picture is quite different: There are broad bands of increased density alternating with bands of normal density on all the long bones of the body and on the ilium and the scapula. They vary in appearance on the different bones only in their breadth, which variation corresponds exactly to the relative rate of growth of the various bones, being broadest on the bones that grow most rapidly.

The feeding of cod liver oil and phosphorus will produce dense transverse lines, but they do not have the breadth of these bands. In this condition the formation of the bands does not correspond to the periods when cod liver oil and phosphorus were given, nor to the infections the children have had.

So far as I know, there is as yet no adequate explanation for the formation of these bands. But undoubtedly, at least to my mind, they must depend on some constitutional peculiarity of the child itself, probably an endocrine unbalance. The child responds in an abnormal way to the factors producing temporary cessation of the growth of bone. An exaggerated form of the normal *Grenzscheide*, the peculiar cartilage ground substance or matrix with its strong affinity for calcium, continues to be laid down over a longer period of time, and, as a result, these broad dense bands are left behind on the shaft.

DR. IRWIN RUBELL: Except for the recognized tuberculosis, this child presented no abnormalities. If a constitutional inferiority and hypothyroidism were present, they were not clinically demonstrable, either in the patient or in the immediate relatives.

THE TREATMENT OF THE FUNCTIONAL DISORDERS OF INFANCY WITH DESICCATED SUPRARENAL AND THYROID (Inaugural Thesis). DR. ORVILLE BARBOUR.

Believing that the information at hand justified an investigation of the possible merits of endocrine therapy, I have endeavored to determine, to my own satisfaction at least, the clinical value of such treatment. During the past three years I have administered desiccated whole gland substances of both suprarenal and thyroid to infants whose manifestations of aberrant function could not be ascribed to demonstrable pathologic changes or directly to the nature of the food. If used in appropriate dosages, desiccated suprarenal seems to relieve most of the functional disorders. Each patient with respiratory and circulatory disturbances shows almost immediate improvement following desiccated suprarenal therapy, and subsequently complete relief occurs with the continuance of the medication. The gastro-intestinal symptoms with the exception of constipation also are usually promptly relieved following the proper administration of the desiccated suprarenal substance. The glandular material is also the most effective remedy which I have used in the treatment of eczematous lesions of the skin. The nervous irritability which is frequently seen in this type of patient is usually allayed after the administration of desiccated suprarenal. In each of the disorders except in diarrhea desiccated thyroid seems, in some cases, to have a beneficial action in combination with the desiccated suprarenal. In relation to gastro-intestinal activity, the influence of the two glandular substances appears to be somewhat antagonistic. Desiccated thyroid seems to promote gastro-intestinal activity, whereas desiccated suprarenal seems to inhibit it. Fetter and Carlson have recently demonstrated experimentally the stimulating action of the thyroid gland on the gastro-intestinal tract. On account of our ignorance regarding the normal physiology of the suprarenal cortex and medulla, one would hardly be justified in attributing the clinical effects of the desiccated suprarenal substance definitely to either the medullary or the cortical portion. We do not have sufficient reasons for the selection or exclusion of the one or the other. Furthermore, until pure extracts or hormones (other than epinephrine) of either component are generally available, we have little choice in the matter. Therefore, I believe that unless my clinical results are disproved or until a medullary or a cortical product becomes clearly indicated and generally available, one is justified in using the extract of the whole gland.

My usual practice is to prescribe desiccated suprarenal initially. If the patient's condition does not improve promptly after the administration of desiccated suprarenal in optimal dosage, I find that combining its use with that of desiccated thyroid almost invariably brings about the desired results. Since the various symptoms tend to be exaggerated after meals, better results are obtained when the endocrine extracts are given with or preceding the feedings. And the more concentrated the food, the more of the glandular substances will be required in the beginning, but the more complete the food, the less long will they be needed. The doses which appear to be effective are from 0.016 Gm. (¼ grain) to 0.06 Gm. (1 grain) of desiccated suprarenal gland and from 0.008 Gm. (⅛ grain) to 0.016 Gm. (¼ grain) of desiccated thyroid gland. The amount of the dose and the frequency of administration depend on the severity and duration of the symptoms, the age and size of the patient, the quality and quantity of the food and the number of feedings in twenty-four hours. Symptomatic relief may at times be obtained more quickly if atropine or phenobarbital is also given. Increasing experience, however, is teaching me that desiccated suprarenal and, in constipated patients, desiccated thyroid are more effective than are any of the other remedies in our armamentarium. The substitutional therapy, if it proves to be such, being more of a specific treatment, seems to me to be a more desirable choice. One is at least probably administering mineral and chemical compounds which are not foreign to the body tissues and which not only are or should be a part of the infant's food but probably are essential to the maintenance of physiochemical equilibrium.

The length of time the patients seem to require the glandular material varies from one to six months. The earlier the condition is recognized and treatment

instituted, the more prompt and effective is the treatment. The ignoring or overlooking of snuffles, a slight cold, a spitting up of food, colic and other apparently minor disturbances is, in my opinion, not justifiable.

The only untoward manifestation that I have seen following the ingestion of desiccated suprarenal is a drowsiness somewhat similar to but never as profound as that produced by phenobarbital. In the very few cases in which this has occurred, the condition promptly cleared up, and by decreasing the dosage or by combining desiccated thyroid with desiccated suprarenal the recurrence of the reaction seems to have been prevented.

One of the most gratifying results of endocrine therapy has been the subsequent freedom from disease and the better physical condition of the infants who received that therapy compared with that of children with manifestations of a diathesis who have not received the glandular treatment.

DISCUSSION

DR. ANDREW C. IVY (by invitation): I should much prefer to hear a clinician discuss this paper than to discuss it myself, because I believe that it is primarily a clinical paper. My clinical experience in pediatrics is very limited.

I presume that I am expected to discuss the relation of the suprarenal glands and the thyroid gland to the gastro-intestinal tract, and the rationale of the endocrine therapy that has been used.

First, let us consider the relation of the suprarenal glands to the gastro-intestinal tract. When animals from which the suprarenal glands have been removed are examined at necropsy, the chief gross changes are found in the gastro-intestinal tract. They consist of ecchymotic hemorrhages in the gastro-intestinal mucosa. We get the impression that these hemorrhages are due to spasm, but cannot be positive of that. Not infrequently we find blood in the lumen of the bowel, and we may observe melena. Examination of the pancreas shows it to be hyperemic and congested. When the animals live from fourteen to twenty-five days, owing to the therapy or to other causes which I shall not enumerate, we have observed that they have alternate attacks of constipation and diarrhea, anorexia and, possibly, vomiting. In addition to this, they manifest mental symptoms which in the dog are somewhat similar to hallucinations in man; they have barking fits and may have convulsions. Examination of the blood shows a tendency to concentration, a low blood sugar content and a lower content of sodium than is generally found.

As to whether or not the administration of extract of desiccated suprarenal by mouth has any effect on the motility or on the secretory activity of the bowel, I cannot state definitely. So far as I know, no observations have been made on the effect which the giving of suprarenal extract by mouth has on the motility of the intestine. Many observers have shown that epinephrine is inhibitory when given parenterally. There are reports stating that if epinephrine is placed in capsules and fed with meals, gastric secretion is increased. My own experiments on dogs have shown that when epinephrine is given by mouth, no increase in secretion is observed as a rule, although it may occur. If too much is given, nausea and vomiting result.

I am referring to epinephrine because Dr. Barbour has told me that he uses the Parke Davis tablets, which, I am informed, contain epinephrine. These tablets may exert a temporary local effect on the stomach, but epinephrine decomposes rapidly in the intestine. When taken by mouth, epinephrine has little, if any, systemic action. However, we cannot state on the basis of the laboratory evidence that the epinephrine in these tablets has no effect on the infant. Actual studies on the infant must be made before this question can be answered.

There may possibly be some cortin in these epinephrine tablets, although I doubt that there is. Four or five years ago, I should have stated that there was no evidence that epinephrine given by mouth is active. Since then, Marine, Rogoff and others have reported that it is active when given by mouth. Cortin has not been shown to be present in the tablets used by Dr. Barbour, so we can only speculate in this regard.

Judging from the amount of suprarenal cortex that has to be given to an adrenalectomized cat to keep it alive and from my knowledge of the chemistry of the active principle, I should state that not much cortin is present in these tablets, but we must keep in mind that Dr. Barbour is dealing with infants, and that in the laboratory and in cases of Addison's disease we are dealing with adults. We must keep our minds open to possibilities.

It is an established fact that small doses of thyroid extract have a tonic action on the gastro-intestinal tract. Large doses depress secretion and cause marked diarrhea. One should not be surprised to observe a relief of constipation and possibly an improvement in appetite and digestion when small doses of thyroid are given to a constipated infant. However, I have always taught my students in physiology that before they give thyroid extract they should ascertain the basal metabolism of the patient and should follow it during the administration of thyroid, and that the basal metabolism is the true indication for the administration of thyroid extract and for the control of the amount of the extract that should be given. It is unfortunate, as I see it, that we do not have some easily utilized method for doing basal metabolic tests on infants. If we had, we might be able to obtain more positive data in regard to the type of cases to which Dr. Barbour refers.

I think I should point out that there may be some truth in the idea that a suprarenal or thyroid constitutional disturbance may be present in the cases Dr. Barbour has reported. To show that this is worth considering, I should like to refer you to the views of two well known pathologists, Warthin and Marine. (These views were outlined, but they are omitted from this report of Dr. Ivy's discussion.)

Other points of interest to pediatricians have developed in regard to suprarenal and thyroid physiology. Recently Webster and Chesney found that by feeding rabbits a certain type of cabbage, marked hyperplasia of the thyroid gland could be produced. Marine has shown that this diffuse hyperplasia of the thyroid can be prevented by the administration of iodine and by the feeding of extracts rich in vitamin C, now believed to be one of the hexuronic acids, which is one of the building stones of connective tissue. The suprarenal is related to vitamin C. If animals are placed on a diet deficient in vitamin C, the suprarenals hypertrophy, and hexuronic acid, which these glands contain in relatively large amounts, disappears.

Within the last few weeks, Hartman, who has done so much of the work on cortin, has reported that he made an extract of the suprarenal cortex which is free from hexuronic acid, but which if given to animals on a diet deficient in vitamin C will delay the onset of scurvy. We cannot at this time speak authoritatively in regard to the relative activity of the suprarenal gland and the gastro-intestinal tract. Dr. Barbour has been careful to point out that his use of the suprarenal extract in these cases is strictly empirical, and I think that he should be complimented for his caution in this regard.

DR. HENRY E. IRISH: When Dr. Barbour's paper was submitted to the executive committee for approval as an inaugural thesis, considerable discussion was raised as to whether or not it was of the type that should be presented as an inaugural thesis. It was conceded that the work showed sincerity and activity in observation, but a minority of the committee, including myself, was unable to reconcile the statements submitted with the established dictum of pharmacologists, that suprarenal extract administered by mouth is not effective. Consequently, I referred this question to various persons in whom I expected to find such extensive knowledge as would enable them to give me an idea of the present-day views of such matters, and I was informed by the Council on Pharmacy and Chemistry of the American Medical Association that, so far as is known, there is no literature which shows that suprarenal extract administered by mouth has any effect. Dr. Bernard Fantus confirmed that view, and textbooks of pharmacology, one after another, very definitely reaffirmed it. Then I took up the matter with Dr. William Peterson of the University of Illinois, and he was not so sure that the question had been settled for all time. His belief was that the question is still open. He

showed me some graphs which he had constructed, presenting certain changes which followed the administration of solutions of suprarenal by mouth; these seemed to him to be of sufficient constancy to indicate that there had been some effect. His suggestion was that possibly epinephrine is not absorbed when given by mouth. It may be true that it is destroyed in the liver; yet, on the other hand, he thought it possible that there is a certain leakage in the passages to account for the effect. He referred me to the head of the department of dermatology who, he said, had been giving suprarenal extract by mouth in certain cases. I consulted Dr. Senear, and he said he felt that clinically certain effects were achieved by giving suprarenal extract by mouth in selected cases; he mentioned in particular certain forms of alopecia, not the ordinary alopecia areata but the types that tend to be permanent. He was of the opinion that patients with these types are affected by the oral administration of epinephrine.

Of course, we are all familiar with Professor Finkelstein's use of epinephrine sublingually in pylorospasm. He was using it as a routine treatment in 1926, when I visited his clinic.

I reported part of this information to the executive committee, and we all agreed that it would be well to have this paper presented and to have the subject open to discussion, in order to get the opinion of the society at large.

Another thing has come to me, namely, that in Europe one finds various hormones and gland extracts used commonly and that there exists a ready acceptance—whether too ready or not I am not sure—of the results achieved. I have been wondering whether the attempts made by institutions, commercial and others, to force our thought along the line of glandular efficacy have not, in a sense, tended to retard a belief that might have been founded on a normal growth from experimental data and on the logical deductions that might be made from such data.

For my part, I thoroughly enjoyed both the paper and the discussion by Dr. Ivy, and my mind remains open.

Dr. George F. Munns : As Dr. Barbour has said, there is some reason to believe that suprarenal insufficiency may be a partial explanation for the occurrence of colic and pylorospasm. Two years ago Dr. Aldrich and I presented before the American Pediatric Society a paper which demonstrated that many of the babies suffering from those disturbances have a low blood sugar content. The low blood sugar content might be explained on the basis of suprarenal insufficiency, or it may be due to a hyperinsulinism or to a low supply of glycogen from the liver. The findings tend to support Dr. Barbour's theory that the administration of epinephrine may be beneficial in these cases. Apparently, Dr. Barbour has secured very good results by the oral administration of desiccated suprarenal glands.

We also know that roentgenotherapy and atropine are of value in the treatment of this condition. Probably all of you have seen a complete and permanent remission of symptoms following a reaction to atropine accompanied by a high fever.

In the treatment of many of the babies with pylorospasm and vagotonia in the Infant Clinic at the Children's Memorial Hospital, we found that practically all of them thrived well on feedings of evaporated milk and $\frac{1}{1.000}$ grain (0.00006 Gm.) of atropine given fifteen minutes before each feeding. It was rarely necessary to continue the atropine for longer than a month. In many instances roentgen treatment produced a marked remission of symptoms.

During the past two years we have felt that vagotonia was occurring less frequently among new-born infants than it had during the "boom" years and we wondered whether perhaps the pace at which we live might not have a definite influence on the incidence of vagotonia. In checking over the charts of the new-born for 1929 at the Evanston Hospital, I found that definite symptoms of vagotonia occurred in about 1 in every 39 babies, while in 1932 the proportion was 1 in every 84. In 1929 there were 25 stillborn babies; in 1932 there were only 8. In 1929 there were 34 deaths among the new-born; in 1932, only 12. There were only about 100 more babies delivered in 1929 than in 1932; the total was 1,573 for the

two years. These figures, I believe, indicate that our mode of living may have a definite effect on the physical condition of the new-born infant.

DR. JOSEPH BRENNEMANN: I feel quite unqualified to discuss this question from either the clinical or Dr. Ivy's standpoint, but when my good friend Dr. Barbour is being biopsied I should like to say a few words.

Whenever a person has somewhat unconventional ideas on a subject the question always arises as to whether he is a prophet or whether he is a little aberrant. I took occasion to tell Dr. Barbour once before that I thought he was a bit "nutty" in some ideas he had long these lines. But when I remember that he was, I believe, the first one to point out a possible connection between the thymus and pylorospasm, and when I listen to what Dr. Ivy has just said, I wonder whether it is not possible that I am the one who is mistaken and not he. It is the history of medicine that things that seem all wrong or aberrant at one time prove at a later time to be correct, and vice versa. The great difficulty in a matter of this sort lies in two directions: It is not always safe to reason from the rabbit and the guinea-pig to the child, and it is always difficult and uncertain to make deductions as to therapy in human beings, as, because of the very nature of the subject, we cannot have a proper control.

Anyway, I think that any one who has as many ideas, as much experience and as much basic information on the subject as Dr. Barbour, even if the ideas are all wrong, should be welcomed into the society.

DR. ORVILLE BARBOUR: You have been very kind to me and to my efforts. No doubt, as Dr. Munns suggested, environmental conditions have their effects on the disorders we discussed. I believe that the diet and health of the mother are also important etiologic factors. If that is true, perhaps the obstetricians could assist in the prevention of these conditions.

To have Dr. Brennemann feel tolerant toward one's ideas is a compliment. I do appreciate it. If we may keep an open mind, and not let our traditional prejudices cloud our vision, perhaps we may succeed in determining the actual place (if any) of the endocrine glands in the etiology and treatment of these little understood disorders. We should at least obtain a better understanding of their physiopathology.

PHILADELPHIA PEDIATRIC SOCIETY

Stated Meeting, March 9, 1933

JOSEPH STOKES, M.D., *President, in the Chair*

USE OF INSULIN AS A STIMULUS TO GROWTH, WITH SPECIAL REFERENCE TO PREMATURE INFANTS. Presented by DR. E. D. ATLEE.

Insulin was first used in the treatment of malnutrition of children in 1924. In this study, insulin was given in small doses of 1 or 2 units per day to ten premature and two mature new-born infants who failed to show normal gains in weight on adequate diets of various formulas of breast milk, lactic acid milk or milk and cereal. All of these patients showed favorable responses as indicated by: (1) increase in appetite and ability to take feedings; (2) increase in weight, and (3) increase in general nutrition.

DISCUSSION

DR. REUBEN DAVIS: After hearing this interesting discussion and case report on the use of insulin in premature infants, there is one important question that presents itself, and that is, what effect is exogenous insulin going to have on endogenous insulin or on the function of the islands of Langerhans? The islands function most when stimulated, and carbohydrate is the stimulating factor. If

insulin is supplied from an outside source, it is conceivable that the islands might cease to function. Work has been done on this subject, however, and it was found that such is not the case. At first there is a temporary fall of carbohydrate tolerance, but at the end of the second week a dextrose tolerance test discloses an actual increase in the secretion of endogenous insulin.

In regard to the physiologic actions of insulin, the storage of water is of particular interest. For each gram of carbohydrate stored as glycogen, there is 3 Gm. of water stored. The edema that develops in some persons with diabetes during treatment and the miraculously rapid rate at which carbohydrate is absorbed in the gastro-intestinal tract during hypoglycemic states indicate that there is an increased permeability of the cells throughout the body. The accelerated storage of glycogen and the increased permeability of the body cells explain the storage of water.

The fact that patients receiving insulin maintain weight after the administration of insulin has been discontinued shows that the increase is due only in part to the storage of water and that it must result in part from a deposition of fat. I agree with Dr. Atlee that even with such small doses as from 1½ to 2 units the danger of shock should be borne in mind, and that the material should be kept at hand to administer dextrose intravenously.

PEDIATRIC STUDIES OF PULMONARY SUPPURATION AND FOREIGN BODIES. DR. S. GOLDBERG and DR. NATHAN LEVIN.

These studies deal mainly with the importance of physical signs in relation to foreign bodies, to bronchiectasis, to pulmonary suppuration and to other intrapulmonary conditions as encountered in the Jackson Bronchoscopic Clinic. Roentgenograms illustrating the part that the roentgenologist plays in making the diagnoses were shown.

The various other clinical manifestations are emphasized which make it possible to detect these conditions at an early stage, thereby permitting a much more favorable prognosis. Cases showing the value of early diagnosis are cited and contrasted with cases that went undiagnosed for a long period of time and showed a marked tendency to chronicity.

DISCUSSION

DR. CHEVALIER L. JACKSON: I think that the lesson from this presentation is that the bronchoscopist needs both the pediatrician and the roentgenologist. The impressive roentgenograms presented show the phenomena of obstructive emphysema and atelectasis. Such information as that one certainly wants to have. One should never omit roentgen examination even though it will not show the shadow of a nonopaque foreign body. Likewise, one must not neglect the physical examination, because if the roentgen findings are inconclusive, some of these other signs that Dr. Goldberg has given may be present. Since this is a meeting of pediatricians, I should like to present a recent case which illustrates the importance of examination by a pediatrician.

A child, 4½ years of age, came to the clinic with a history of having choked on salted peanuts. He was wheezing and was spitting up slightly blood-stained secretions. Some fragments of peanut had been removed, and the child had coughed up several more. Dr. Levin and Dr. Perlman both examined the boy, and in spite of the fact that the roentgen examination showed practically nothing abnormal, they thought that bronchoscopy should be done. It was done and several large fragments of peanut were found.

ABDOMINAL CATASTROPHES OF THE NEW-BORN. Presented by DR. W. H. CRAWFORD.

Acute abdominal conditions of the new-born are more common than one is apt to think. In this class, congenital malformations are most common. Recent literature contains more and more reports of such catastrophes as ruptured gastric

ulcer, perforated duodenal ulcer, intussusception, rupture of the liver and other viscera from injuries received at birth, volvulus and peritonitis from various causes. In 1931-1932 at the Philadelphia Lying-In Hospital 4,172 children were born, ten of whom showed such abdominal conditions.

Hemorrhage into the peritoneal cavity owing to injury of the liver occurred in one infant and retroperitoneal hemorrhage from a rupture in the region of the left kidney in another. Striking in the histories of these two infants is the rather sudden onset of symptoms several days after birth. Rupture of a gastric ulcer on the eighth day of life, with death following a few hours after operation, occurred in a third infant. In one infant death was due to peritonitis without etiologic explanation, and in another, to rupture of abscesses of the kidney.

Five of the ten cases were manifestations of congenital defects of the gastrointestinal tract. These were: (1) failure of rotation of the stomach, with obstruction at the pylorus caused by kinking; (2) complete atresia of the duodenum; (3) strangulated right inguinal hernia; (4) herniation of the intestine through an abnormal opening in the mesentery, and (5) imperforate anus.

DISCUSSION

Dr. W. Wayne Babcock: Dr. Crawford introduces fairly unusual congenital involvement in the new-born and the important associated surgical problems. As to intra-abdominal hemorrhage, blood is absorbed so rapidly from the infant's peritoneal cavity that limited effusions of blood without other complication are best treated without surgical intervention. Progressive bleeding from the liver, spleen or other viscera involves a greater hazard in the necessary operative control than in the adult. Extraperitoneal hemorrhage in the child, as in the adult, is usually best treated conservatively. Particularly is this true with hemorrhage from the suprarenal glands or kidneys.

Occasionally serious hemorrhage, difficult to control, may occur at the umbilical stump. I recall one baby whose life was saved by the old-fashioned expedient of running two needles at right angles through the stump and then winding a bit of string under the needles. Ulceration, hemorrhage and perforation of the intestine of the baby suggest the presence of ectopic portions of gastric mucous membrane, which are most often found in Meckel's diverticulum. For perforation, at least, immediate surgical intervention is demanded.

Congenital stenoses of the alimentary canal usually occur at the ends of the intestinal tube. The common obstructions of the rectum and anus may usually be tunneled or broken through from below. The new-born child stands enterostomy or intestinal anastomosis poorly, although one of Dr. Crawford's little patients recovered after a colostomy. Torsion of the stomach presents a difficult surgical problem, and an attempt should first be made to keep the stomach continuously empty by constant light aspiration or an indwelling tube. It is difficult to make an anastomosis with the intestine hardly larger than the brachial artery. For an early intussusception Rehn's method of injecting barium sulphate under low pressure while manipulation is being made under the fluoroscope may be successful. Rather rarely, intussusception may recur and have spontaneous relief many times. With congenital obstructions in the duodenum or proximal jejunum the symptoms usually develop promptly after birth, without the delay associated with hypertrophic stenosis of the pylorus and without the olive-shaped mass found in that condition. With obstructions below the ampulla there is vomiting of bile; with those above it no bile is vomited and the condition resembles pyloric stenosis. With obstructions lower in the intestines the onset of symptoms may be delayed. Thus, a baby sent to the hospital with atresia of a segment of the ileum when 18 days old nursed rather normally during the first two weeks of life. Partial congenital obstructions may continue to give trouble for many years. Recently, but in an older child, my associates and I saw an intussusception of the jejunum which had recurred not less than fifteen times; the condition was permanently relieved by the removal of an adenoma higher up in the jejunum which had been overlooked at two previous operations.

When the abdomen of a baby is to be operated on, the child is bound to a well padded board, and local anesthesia is used. If the infant is given an old-fashioned sugar tit moistened with a little paregoric or whiskey it continues to suck and often will not cry even during a very serious operation.

DR. W. EMORY BURNETT: This report was interesting and dealt with some rare conditions. The types which one sees most often are congenital. These little patients stand surgical intervention rather poorly. The fact most evident from this report and from personal experience is that most of them do not have the opportunity offered by surgical intervention early enough in the disease. The diagnosis in such cases is difficult, but if it could be made a little sooner or, at least if exploration could be done a little sooner, the end-results might be much better. Most of these infants are fatally ill, but by early operation the mortality statistics might be improved materially. The most recent case that I have seen was one of imperforate anus that had been opened immediately after birth. When the child was 8 years of age, it was found to have a fistula leading from the rectum into the urethra, undescended testicle and a multiplicity of other lesions. The fistula was closed and the other anomalies are being corrected. I should like to see such patients benefit earlier from surgical intervention, and believe that mortality in such cases might be reduced thereby.

DR. PAUL MORRIS: One interesting condition mentioned briefly was that of suprarenal hemorrhage. Dr. Babcock mentioned that there was not much to be done in such cases. I think that that is true of surgical treatment.

There is one disturbing factor in therapy. One must suspect the diagnosis, and that is rather difficult. The hemorrhage may form a tumor so large that it is palpable. Other symptoms that the child usually presents are marked pallor, fever and unusual cyanosis, unless the pallor masks the cyanosis. With such infants, therapy has been aided by administering extract of suprarenal cortex. By this means the infant is tided over the dangerous period until the hemorrhage has been absorbed and the suprarenal gland has had a chance to recover its normal function.

BLOOD STUDIES IN THE NEW-BORN. Presented by DR. F. KONZELMANN.

Experience and the literature have shown that the normal infant's blood picture shows marked variation, especially during the first few weeks of life. There are two curves of variation. One corresponds to a slow process affecting chiefly the hemoglobin, which reaches its lowest point about the end of the first year. It is almost 23 Gm. at birth and falls to 12 Gm. at one year. The number of red cells rises and then falls during the first eighteen hours, becoming constant at thirty hours at slightly over 5,000,000. The other curve relates to a daily change which affects chiefly the leukocytes. The total count at birth is 16,000. It rises to 21,000 at six hours and falls gradually to 9,000 at five days. The polymorphonuclear count follows closely the total count at a slightly lower level. The lymphocyte count is about 7,500 at birth; it rises slightly and then falls to 4,800 at forty-eight hours. After this there is a gradual rise, until a figure is reached which exceeds the polymorphonuclear leukocyte count. The monocyte curve follows the lymphocyte curve closely. Differences in technic seem to alter the values. The use of supravital stains reveals monocyte counts of over 1,000 while by the ordinary technic the values hover below 500 per cubic millimeter. These variations suggest the adoption of a definite system for studying the blood of the new-born, such as: (1) to post in the ward a chart of normal counts for each of the first five days and for each week of the first month and each month of the first year; (2) to speak of hemoglobin values in grams per hundred cubic centimeters of blood instead of in percentages of normal, wherein the value of 100 per cent either is a variable or is not known; (3) to speak of the various white cells in absolute numbers per cubic millimeter instead of in percentages of the total white cell count, thus making unnecessary such terms as "relative lymphocytosis"; (4) to take all counts for comparative study at approximately the same time each day, for example, between

7 and 11 a. m.; (5) to make several counts at intervals, for dependence should not be placed on a single observation; (6) to use the cover glass method of making blood smears when time and technical assistance permit, since it is far more accurate than the commonly practiced slide method; (7) to use the supravital staining technic when a study of monocytes is of importance.

NATIONAL RESEARCH COUNCIL, DIVISION OF ANTHROPOLOGY AND PSYCHOLOGY, COMMITTEE ON CHILD DEVELOPMENT

Chicago, June 22-24, 1933

R. S. WOODWORTH, *Chairman, Committee on Child Development*

A. T. POFFENBERGER, *Chairman, Division of Anthropology and Psychology*

FOURTH CONFERENCE ON RESEARCH IN CHILD DEVELOPMENT

INDIVIDUAL ADAPTATION TO THE SOCIAL ENVIRONMENT. A. R. RADCLIFFE-BROWN.

The development of a child may be considered a combination of two processes, physical growth and social conditioning. Each of these may be divided into constant factors common to the human race and variable factors peculiar to particular races, groups or individuals. For a thorough theoretical understanding of child development it seems essential to study the process comparatively in different social environments. For this purpose a more satisfactory technic is needed—one which will permit application to groups markedly different. Child development should be treated from the standpoint of a systematic study of the nature of the adaptation of the individual human being to the social environment. The ethnologist may render valuable cooperative assistance to this end.

EMERGENCE OF THE CONCEPT OF PERSONALITY IN A STUDY OF CULTURE. E. SAPIR.

Interest in human behavior vascillates between that which is imputed to the group culture and that which is imputed to the individual. The interpretation of a particular observer is based on the idea and action patterns of the interrogated person or on those of the interpreter himself. Cultures as ordinarily represented are abstracted configurations of these patterns and have many different meanings for the several persons in the group.

From the standpoint of the child, culture is not given but gradually discovered, and he accepts its various elements with many different meanings, the end-result being influenced by the reaction between his own personality and the personalities of those with whom he comes in contact. Sapir suggests that the child be studied carefully until the age of 10, with a view to seeing the order in which cultural patterns or parts of patterns appear in his psychic world and the relevance of these patterns to the development of his personality, and, finally, how much of the total official culture has significance for him.

STANDPOINT AND METHODS OF SOCIOLOGY IN THE STUDY OF PERSONALITY AND SOCIAL GROWTH. E. FARIS.

Faris' point of view may be summarized in his own words: ". . . . habits, made explicit in the personality. . . . The elements of the individual person-

ality, therefore, are not found in the individual person, but are to be sought in the mores of the group as these are appropriated, accepted, rejected or modified in the interaction." With this concept the group becomes the "prior reality," from which standpoint a study of the group is valuable in learning of the growth of personality which takes place in children of a given society. An example of the sociologic-technical method is supplied by Faris from reports of unfinished investigation on the problem of punishment.

SOME CHARACTERISTICS OF THE SOCIOLOGIC APPROACH TO PERSONALITY. LOUIS WIRTH.

Recognizing that the sociologic approach is only one of many special fields, Wirth presents an argument which gives importance to the complex factors of culture in the development of personality. Both the individual's consideration of himself—his rôle—and the effect of his reaction to the rôle to which his associates assign him are emphasized. With reference to the child, a distinction is made between the physiologic and the psychologic organism and a person who consciously plays rôles. Wirth also suggests a division between the preverbal and the verbal period as being of more significance than one between the preschool and the school age. Although culture is important, personal experiences are considered the most fruitful for studies of personality by the sociologist.

SOCIAL AND PHYSICAL FACTORS IN DEVELOPMENTAL AGE. PAUL HANLY FURFEY.

Summarizing a number of published and unpublished studies about the concomitants of the developmental age of boys, Furfey finds the following tentative conclusions. The developmental age bears considerable relation to puberty and to home conditions, the developmental quotient increasing as the boy reaches adolescence and decreasing with overprotection in the home environment. There seems to be some relation to the following factors: dental age, mental age and socio-economic status. There does not seem to be any relation between developmental age and physical measurements, carpal ossification, race, residence in particular parts of the country, delinquency, companionship and position in the family.

THE FAMILY AS A MEDIATING FACTOR IN THE ADJUSTMENT OF THE CHILD. G. D. STODDARD.

Concepts of the family as a mediating factor may be analyzed as follows: (1) its influence on the communal or other social forces; (2) its importance as a sole or primary source of information, practice or attitude believed to affect adjustment; (3) its inheritance of habit or attitude traceable through several generations; (5) its influence measurable in terms of the adjustment of the child.

The author is impressed with the advantages which might accrue to investigations of this sector of personality by frank allocation of certain aspects of the entire problem to scientific method although it cannot be expected to preempt all of the territory. The extent of correlation of certain well chosen factors or the subdivision of large group classifications in existing studies emphasizes the practicality of the suggestion. No single factor seems responsible for maladjustments.

RELATION OF DIFFERENTIAL ENVIRONMENTS WITHIN A GIVEN CULTURE TO CARE OF THE CHILD. JOHN E. ANDERSON.

Data were obtained by questionnaire on 3,779 children in 2,758 white families and 321 children in 202 Negro families by a sample method of wide geographic distribution. The families were divided into seven socio-economic classes. An analysis of the data revealed that the evidence of the existence of differential environments so far as the child is concerned is overwhelming. When the population is divided on the basis of socio-economic status and the practices of

the resulting groups are studied in detail, a picture is obtained of a society composed of a series of cultures, each of which differs from the ones immediately above and below it and all of which are arranged in a linear series.

THE CONCEPT OF INTELLIGENCE AS A FIXED OR UNMODIFIABLE FEATURE OF THE PERSONALITY. FRANK N. FREEMAN.

Freeman feels that intelligence is modifiable. After presenting quotations from Binet to support his contention and criticizing the interpretation of the usual comparisons between groups, he offers data from several studies which through the nature of the material and controls offer substantial evidence of the modifiability of intelligence by environmental influence largely of an educational character. Mr. Freeman is impressed with the value of the genetic method of study, that of tracing the course of intellectual development of children either singly or in groups with a view to discovering the factors which produce it, as contrasted with studying the results of the development as evidenced by performance, as is done in adult intelligence tests.

Book Reviews

Histopathology of the Peripheral and Central Nervous Systems. By George B. Hassin, M.D. Price, $6. Pp. 491, with 229 illustrations. Baltimore: William Wood & Company, 1933.

This book, the third in its field to be published in this country within the past year, fills a long-felt want, although incompletely. Interest in neuropathology has been very active in recent years in America as well as elsewhere, and has resulted in a great deal of creditable work, but there has heretofore been almost no systematic treatment of the subject as a whole in the English literature. Moreover, the microscopic pathology of the nervous system receives scant attention in textbooks of neurology and general pathology alike.

Written as a special text on pathology, the scope of the work is enormous, and necessitates very brief treatment of much of the material in spite of the deliberate omission of any separate consideration of the general aspects of the subject or of clinical correlations. Certain phases, some of which would be of interest to pediatricians, receive inadequate mention or none at all, such as the malformations, infantile diplegias and the histopathology of the amentias. Yet, much that is of importance to those interested primarily in children's diseases is included: hereditary degenerations of the spinal cord, infantile forms of amyotrophy, encephalitis, progressive degenerations of the brain, including Schilder's disease, amaurotic idiocy, Niemann-Pick disease, tuberous sclerosis and, of course, tumors. The brevity is to some extent compensated for by a very full working bibliography, notable in that it contains references to the original articles of fundamental importance in the older literature, as well as to the contemporary contributions.

In places the context of the work is strongly influenced by the author's own personal slants on the subject. His well known concepts of the toxidegenerative nature of multiple sclerosis and of the rôle of epidural infiltrations in the production of degenerations of the spinal cord, especially in tabes, and notably his doctrine of the origin of spinal fluid from the brain and cord and its absorption along the perineurial spaces receive emphasis. This forms an unfortunate bias in the work, since in no case do these ideas rest on so sure and uncontested a footing as one might be led to believe. On the other hand, his discussion of tumors is based on a broader point of view than is ordinarily encountered at present. While the majority of his figures of gliomas are taken from Bailey's preparations, he does not limit his classification rigidly to that of Bailey and Cushing, but gives due consideration to the views of the French school and of Lotmar. The book is richly illustrated by photomicrographs, many of them from the author's own large and excellent collection.

Thérapeutique hydro-climatologique en pédiatrie. By P. Nobécourt and G. Boulanger-Pilet. Price, 22 francs. Pp. 193. Paris: Masson & Cie, 1933.

This publication is designed to assist physicians in choosing and recommending the proper European stations and spa's where climatic and hydrotherapeutic measures may be obtained favorable to the various disturbances of infants and children. In part I the various diseases of children amenable to this type of treatment are discussed with suggestions concerning the places in which the climate, mineral waters and baths are best suited to the particular illness, age and disposition of the patient. These directions are very explicit and detailed. In part II the composition of various mineral waters is explained and their therapeutic action discussed. Part III consists of a list of the principal stations with data on each concerning the climate, altitude, open season, facilities offered and types of illnesses for which they are especially beneficial.

Directory of Pediatric Societies

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor Taillens, Lausanne, Switzerland.
Secretary: Dr. P. Oltramare, rue Decandolle, Geneva, Switzerland.

FOREIGN

Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. Leonard G. Parsons, 58, Calthorpe Road, Birmingham, England.
Secretary: Dr. W. G. Wyllie, 33, Wimpole St., W. 1, London.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman Dr. Alfred A. Walker, Highland Plaza Apartments, Birmingham, Ala.
Secretary: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Place: Cleveland. Time: June 11-15, 1934.

American Academy of Pediatrics

President: Dr. John Ruhrāh, 11 E. Chase St., Baltimore.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Place: Cleveland. Time: June 11-12, 1934.

American Child Health Association

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. Philip Van Ingen, 125 E. 71st. St., New York.

American Hospital Association, Children's Hospital Section

President: Mr. Robert Witham, Children's Hospital, Denver.
Secretary: Miss Agnes O'Roke, Kosair Crippled Children's Hospital, Louisville, Ky.
Place: Philadelphia. Time: Sept. 24-28, 1934.

American Pediatric Society

President: Dr. Charles A. Fife, 2104 Spruce St., Philadelphia.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid, St. Louis.
Place: Asheville, N. C. Time: May, 1934.

Canadian Society for the Study of Diseases of Children

President: Dr. H. P. Wright, 1509 Sherbrooke St. W., Montreal.
Secretary-Treasurer: Dr. R. R. Struthers, 1414 Drummond St., Montreal.
Place: Kingston, Ontario. Time: June, 1934.

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* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

Society of Pediatric Research

President: Dr. Rustin McIntosh, College of Physicians and Surgeons, Columbia University, New York.
Secretary-Treasurer: Dr. Charles F. McKhann, Harvard Medical School, Boston.
Place: Atlantic City, N. J. Time: May, 1934.

SECTIONAL

North Pacific Pediatric Society

President: Dr. Arthur H. Gray, 1117 Second Ave., Seattle.
Secretary: Dr. Raymond H. Somers, Cobb Bldg., Seattle.

Southern Medical Association, Section on Pediatrics

Chairman: Dr. Hugh L. Dwyer, 406, W. 34th St., Kansas City, Mo.
Secretary: Dr. Luther W. Holloway, 117 W. Duval St., Jacksonville, Fla.

STATE

Alabama Pediatric Society

President: Dr. C. E. R. Parker, 401 S. Court St., Montgomery.
Secretary-Treasurer: Dr. John W. Simpson, 1117 S. 22d St., Birmingham.

Georgia Pediatric Society

President: Dr. Joseph Yampolsky, 311 Doctors Bldg., Atlanta.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Place: Augusta. Time: May, 1934.

Louisiana State Pediatric Society

President: Dr. Cecil O. Lorio, 245 Third St., Baton Rouge.
Secretary-Treasurer: Dr. Maud Loeber, Tulane University, New Orleans.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. Adolph G. De Sanctis, 12 E. 11th St., New York.
Secretary: Dr. George M. Retan, 459 James St., Syracuse.

Michigan State Medical Society, Pediatric Section

Chairman: Dr. W. A. Collins, 103 W. Burdick St., Kalamazoo.
Secretary: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Place: Battle Creek. Time: September, 1934.

Nebraska Pediatric Society

President: Dr. W. O. Colburn, 724 Sharp Bldg., Lincoln.
Secretary-Treasurer: Dr. C. G. Weigand, 1614 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Second Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

North Carolina Pediatric Society

President: Dr. J. Buren Sidbury, 15 N. Fifth St., Wilmington.
Secretary: Dr. E. K. McLean, 121 W. Seventh St., Charlotte.
Place: Various children's hospitals. Time: Twice a year.

Oklahoma State Pediatric Society

President: Dr. Clark H. Hall, 117 N. Broadway, Oklahoma City.
Secretary: Dr. M. J. Searle, 108 W. 16th St., Tulsa.

South Carolina Pediatric Society

President: Dr. J. I. Waring, 77 Rutledge Ave., Charleston.
Secretary-Treasurer: Dr. Julian P. Price, Medical Bldg., Florence.

Tennessee State Pediatric Society

President: Dr. Owen H. Wilson, 706 Church St., Nashville.
Secretary: Dr. Joe T. Smith, 702 Medical Arts Bldg., Knoxville.
Place: Chattanooga. Time: April, 1934.

Texas Pediatric Society

President: Dr. Sidney R. Kaliski, Moore Bldg., San Antonio.
Secretary-Treasurer: Dr. Frank M. Martin, 321 Medical Arts Bldg., San Antonio.

Virginia Pediatric Society

President: Dr. Thomas D. Jones, Medical Arts Bldg., Second and Franklin Streets, Richmond.
Secretary: Dr. W. A. McGee, 2618 Grove Ave., Richmond.
Place: Alexandria. Time: October, 1934.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. R. C. Hood, 428 W. Pike St., Clarksburg.
Secretary: Dr. Russell C. Bond, 1325 Chapline St., Wheeling.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. J. A. Garvin, Carnegie Medical Bldg., Cleveland.
Secretary: Dr. William M. Champion, 2323 Prospect Ave., Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. Gladys Boyd, 56 DeLisle St., Toronto.
Secretary: Dr. Lawrence Murray, 1870 Bloor St., W., Toronto.

Bronx Pediatric Society

President: Dr. Morris Gleich, 9 Post Ave., New York.
Secretary: Dr. Harry D. Pasachoff, 1560 Grand Concourse, New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

Brooklyn Pediatric Society

President Dr. Carl H. Laws, 12 Pierrepont St., Brooklyn.
Secretary: Dr. Lewis A. Koch, 62 Pierrepont St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

Central New York Pediatric Club

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Fourth Thursday of October, January and April.

Chicago Pediatric Society

President: Dr. Charles Schott, 48 W. Division St., Chicago.
Secretary: Dr. Bert I. Beverly, 8 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

Dallas County Pediatric Society

President: Dr. P. E. Luecke, 4105 Live Oak St., Dallas, Texas.
Secretary: Dr. R. S. Usry, 1835 Garrett Ave., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

Detroit Pediatric Society

President: Dr. John A. Johnston, 2799 W. Grand Blvd., Detroit.
Secretary: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Secretary: Dr. T. I. Willingham, 478 Peachtree St., N. E., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Intermountain Pediatric Society

President: Dr. Helmina Jeidell, 11 Exchange Pl., Salt Lake City, Utah.
Secretary-Treasurer: Dr. Edwin R. Murphy, 9 Exchange Pl., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month, 8 p. m.

Kansas City (Missouri) Pediatric Society

President: Dr. Hugh L. Dwyer, 406 W. 34th St., Kansas City.
Secretary: Dr. John Aull, 906 Grand Ave., Kansas City.

Memphis Pediatric Society

President: Dr. R. B. McCormick, 1074 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. W. D. Mims, 1024 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

Milwaukee Pediatric Society

President: Dr. T. R. Janney, 1411 Wauwatosa Ave., Wauwatosa, Wis.
Secretary: Dr. John H. Reynolds, 1628 Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New England Pediatric Society

President: Dr. Thomas A. Foster, 131 State St., Portland, Maine.
Secretary: Dr. Gerald Hoeffel, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Martha Wollstein, Babies' Hospital of City of New York, New York.
Secretary: Dr. Harry Bakwin, 132 E. 71st St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northwestern Pediatric Society

President: Dr. Alexander Stewart, 459 Lowry Medical Arts Bldg., St. Paul.
Secretary: Dr. E. F. Robb, 1801 Lyndale Ave., S., Minneapolis.

Philadelphia Pediatric Society

President: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala, Pa.
Secretary: Dr. James E. Bowman, 4091 Comly St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. Henry C. Flood, 119 S. Highland Ave., Pittsburgh.
Secretary: Dr. E. R. McCluskey, Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

Richmond Pediatric Society

President: Dr. W. A. McGee, 2618 Grove Ave., Richmond, Va.
Secretary-Treasurer: Dr. Emily Gardner, 1100 W. Franklin St., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

Rochester Pediatric Society

President: Dr. H. F. Rowley, 176 S. Goodman St., Rochester, N. Y.
Secretary: Dr. J. M. Parker, 26 S. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month from October to May.

Rocky Mountain Pediatric Society

President: Dr. J. A. Schoonover, Republic Bldg., Denver.
Secretary: Dr. Arthur L. Esserman, Republic Bldg., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 7 p. m.

St. Louis Pediatric Society

President: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, Beaumont Bldg., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

Seattle Pediatric Society

President: Dr. Albert S. McCown, 509 Olive St., Seattle.
Secretary: Dr. Frank H. Douglass, Medical-Dental Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 7 p. m.

Southwestern Pediatric Society

President: Dr. James E. Harvey, 60 S. Lake Ave., Pasadena, Calif.
Secretary: Dr. E. Earl Moody, 3780 Wilshire Blvd., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. John F. Sanders, 320 Townsend St., Lansing, Mich.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.
Place: University Hospital, Ann Arbor, Mich. Time: Nov. 23-24, 1934.

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